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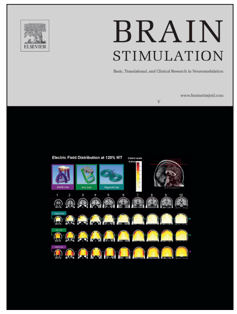

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Jared Cooney Horvath, Jason D. Forte, Olivia Carter

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Quantitative Review Finds No Evidence of Cognitive Effects in Healthy Populations from Single-Session Transcranial Direct Current Stimulation (tDCS)

Jared Cooney Horvath[1]*, Jason D. Forte[1], & Olivia Carter[1]

1 - University of Melbourne, School of Psychological Sciences, Melbourne, VIC, Australia.

Correspondence:

Jared Cooney Horvath

Melbourne School of Psychological Sciences

Redmond Barry Building

University of Melbourne

VIC 3010

Australia

jared.cooney.horvath@gmail.com

Keywords: transcranial direct current stimulation (tDCS); quantitative review; executive function; language; memory; working memory

Abstract

Background: Over the last 15-years, transcranial direct current stimulation (tDCS), a relatively novel form of neuromodulation, has seen a surge of popularity in both clinical and academic settings. Despite numerous claims suggesting that a single session of tDCS can modulate cognition in healthy adult populations (especially working memory and language production), the paradigms utilized and results reported in the literature are extremely variable. To address this, we conduct the largest quantitative review of the cognitive data to date.

Methods: Single-session tDCS data in healthy adults (18-50) from *every* cognitive outcome measure reported by at least two different research groups in the literature was collected. Outcome measures were divided into 4 broad categories: executive function, language, memory, and miscellaneous. To account for the paradigmatic variability in the literature, we undertook a three-tier analysis system; each with less-stringent inclusion criteria than the prior. Standard mean difference values with 95%CIs were generated for included studies and pooled for each analysis.

Results: Of the 59 analyses conducted, tDCS was found to not have a significant effect on any - regardless of inclusion laxity. This includes no effect on any working memory outcome or language production task.

Conclusion: Our quantitative review does not support the idea that tDCS generates a reliable effect on cognition in healthy adults. Reasons for and limitations of this finding are discussed. This work raises important questions regarding the efficacy of tDCS, state-dependency effects, and future directions for this tool in cognitive research.

Keywords: transcranial direct current stimulation (tDCS); quantitative review; executive function; language; memory; working memory

Introduction

Since its modern resurgence at the turn of the century, transcranial direct current stimulation (tDCS) – a noninvasive neuromodulatory device – has been steadily growing in popularity within both the academic and clinical research sectors. Current theory suggests that tDCS, via time-dependent and polarity specific modulation of neuronal firing patterns, can markedly and predictably enhance a number of higher-order cognitions and behaviors. However, a recent systematic review of the neurophysiologic literature undertaken by this group [1] questions the reliability and significance of tDCS effects on all but one neurophysiologic measure tested. Here, we undertake a quantitative review of the cognition literature to determine if tDCS shows a reliable effect on any cognitive tasks.

A Brief Review of Proposed tDCS Mechanisms of Action

tDCS is most commonly delivered via 2 electrodes - 1 anode and 1 cathode - affixed to the scalp overlying cortical regions relevant to the outcome measure of interest [2]. It is believed that passing a weak electric current (typically 0.5-2.0 mA) between these two electrodes modulates neuronal firing patterns in the cortical regions underlying the electrodes via two mechanisms of actions. The first occurs *during* stimulation and involves ionic concentration shifts within the extracellular fluid which serve to modulate neuronal resting membrane potentials thereby hypo- and hyper-polarizing neurons underlying the anode and cathode, respectively [3]. The second occurs *following* long duration (>7min) stimulation and involves long-term potentiation and depression-like mechanisms at the synaptic level thereby effecting hyper- and hypo-communicative activity in neurons underlying the anode and cathode, respectively [3]. To account for these different mechanisms, in this paper we divide studies according to whether the outcome measures were obtained during stimulation (online protocols) or following stimulation (offline protocols).

Quantitative-Review Structure

The poolable cognitive tasks in the literature can be grouped into 4 broad categories: executive functions, language, memory, and miscellaneous. Accordingly, the methods and results sections will be structured around these domains. To be included in this review, the effects of tDCS on a given task must have been explored by at least two different research groups using a comparable tDCS protocol. A full list of studies that assessed the relevant aspects of cognitive function but did not meet these inclusion criteria can be found in Supplemental Material (Figure S1; Table S3). Each poolable outcome measure that satisfied our inclusion criteria is introduced briefly below.

Executive Functions

Executive functions (EFs) are often regarded as a coordinated set of cognitive processes which allow an individual to override more instinctual or automatic responses in order to achieve a specified goal [4]. The following three EF measures met inclusion criteria for this review:

> *Set-shifting:* Individuals must determine which target/s amongst a series of targets are "correct" based on an unspecified rule-set via arbitrarily guessing (eg – red fruit amongst a series of food-

based images). Occasionally, and without warning or explication, the rule-set will change (eg – round vegetables amongst a series of food based images). Improved performance on this task is reflected by a reduction in the time taken to notice this change, abandon the prior rule-set, and learn the new rule-set [5].

Stop signal task: Individuals are repeatedly presented with a target (eg – a visual circle) and asked to respond as quickly as possible each time it appears. Occasionally, however, the target will be paired with a secondary stimulus (eg – an auditory beep); in this instance, the individual should *not* respond to the target. This task is a measure of automatic response inhibition [6].

Stroop task: Individuals are presented with stimuli which contain multiple, uniquely processed dimensions (eg - the word 'red' written in a green colored font), of which the individual must respond to only one. The speed which with a person can accurately respond is a measure of selective attention and goal maintenance [7].

Language

Linguistic-based cognitive tasks utilize language production speed and accuracy to explore the psychological and neurobiological factors that enable humans to produce and comprehend speech ([8]). The following three language measures met inclusion criteria for this review:

Picture-to-word novel-language learning: Individuals are presented with paired images and pseudo-words or words from an unfamiliar language and must learn the pairing of the two. The accuracy with which one can respond to correctly- or incorrectly-joined pairs is thought to be a measure of linguistic learning [9].

Picture naming: Individuals are presented with a series of images (either simple line drawings or photos) and asked to name them as quickly as possible. The time taken to accurately name each object is a measure of lexical access, or 'word-finding ability' [10].

Verbal fluency: Individuals are presented with a phonemic category (eg – the letter 'p') or a semantic category (eg – animals) and asked to name as many words as possible from said category within a specified time limit. The number of words produced is a measure of semantic access [11].

Memory

Memory-based cognitive tasks utilize memorization and recall speed/accuracy to explore the structures and processes involved in the effective storage and retrieval of information ([12]). The following five memory measures met inclusion criteria for this review:

Digit-span recall: Individuals are sequentially presented with verbal strings of numbers which sequentially increase in length and are asked to verbally report the numbers following each presentation. The length of the final number string an individual is able to accurately report back is a measure of digit-span recall WM [13].

<u>*Verbal episodic memory:*</u> Individuals are presented with a list of words several times and asked to memorize it (encoding). Following a delay period (consolidation), during which time the individual is distracted with non-relevant tasks, the individual is presented with 'target' words and asked whether or not each was present in the prior memorized list. The accuracy with which an individual responds to the targets is a measure of verbal episodic recognition memory. An identical procedure, though replacing words with visual images, is utilized as a measure of visual episodic recognition memory [14].

<u>*Visual WM:*</u> Individuals are sequentially presented with a string of visual images. Following each string, a single target is visually presented and the individual must respond whether or not said target was in the prior string. The speed and accuracy with which an individual responds to the target is a measure of visual WM [15].

<u>*N-back WM:*</u> Individuals are presented with a sequential string of stimuli (eg - letters or numbers) and asked to generate a response if a stimulus is identical to the one presented 'N' items prior. The accuracy and speed with which an individual responds to targets is a measure of WM according to the modality of the stimuli utilized [16].

Miscellaneous

An additional four measures met inclusion criteria for this review but could not be grouped into any single cognitive domain:

<u>*Mental arithmetic:*</u> Individuals are asked to complete simple arithmetic math problems in their head. The speed and accuracy with which an individual can complete these problems is a measure of computational efficiency [17].

<u>*Picture viewing/rating:*</u> Individuals are asked to view and rate a series of images of differing valences (typically negative and neutral). The average rating generated within each valence is a measure of emotional processing [18].

<u>*Gambling based risk taking:*</u> Individuals participate in a 'gambling-type' scenario whereby different actions carry varying, yet clearly understood, consequences (eg –choose between two boxes, the first of which has a 90% probability of containing $1 whilst the second has a 10% chance of containing $10). The number of low-probability/high-reward choices an individual selects is a measure of risk-taking propensity [19, 20].

<u>*Rumination:*</u> Individuals are asked to report about the frequency and intensity of mentally generated self-referential thoughts (typically following a pre-arranged negative valence-type scenario, such as receiving a negative grade on an exam) [21].

Methods

Study Selection

Papers included in this quantitative review were obtained from a PubMed database search (June 12th, 2014). The search term “transcranial direct current stimulation” generated 1,156 papers. The abstract of each of paper was then read to determine which outcome measures were included and what type of population was utilized. This initial review narrowed the study pool to 417 (see Supplemental Material: Figure S1 for complete study selection flow chart).

Following this, each article was read and the tasks/outcome measures utilized were noted and organized to identify all outcome measures utilized by at least two different research groups. We chose to exclude measures that have only been replicated by a single research group to ensure all data included in and conclusions generated by this review accurately reflect the effects of tDCS itself, rather than any unique device, protocol, or condition utilized in a single lab. Examples of non-experimentally based systematic errors reliably influencing the results generated by a single research group can be found in all the sciences, from physics (see: [22]), to biology (see: [23]), to medicine (see: [24]). Due to this inclusion criterion, a number of cognitive outcome measures extant in the literature were omitted due to only being reported by a single research group (see supplemental material: Tables S2,). We want to emphasize that this *does not* suggest said research is in any way faulty or incorrect; rather, that inter-group replication is necessary in order to eliminate any potential non-tDCS influential outcome factors.

Next, the stimulation-to-task relationship was determined for each study. As the mechanism of tDCS is thought to differ *during* and *following* stimulation (see above), included papers were divided into those which utilized an ‘online’ protocol and those which utilized an ‘offline’ protocol. Following this, we further divided studies according to the location chosen for the active stimulating tDCS electrode and whether or not anodal or cathodal stimulation was utilized. Finally, all studies not including a sham condition were omitted.

Analysis

Our initial intention was to pool only studies which utilized identical stimulation current densities and electrode montages. However, a look at the results section reveals there is very little direct replication in the literature. Accordingly, we decided to dichotomize current density values (low = 0.0286 mA/cm2; high > 0.0286 mA/cm2) and assessed the respected effects independently.

Next, continuous mean and variation data was extracted from each included study. If continuous numerical data was not included, values were extracted from included images (achieved by exporting images to an image editing program, overlaying a standardized grid, and counting relevant values by hand). For each included study, active stimulation values were compared to sham (control) values and a standard mean difference (SMD) with 95% confidence interval (95%CI) effect size was determined. These values were grouped and analyzed using two different meta-analytic software tools to ensure accuracy (Comprehensive Meta-Analysis - v2.0, Biostat, Englewood, NJ, USA; MetaEasy – v1.0.4, Statanalysis, Manchester, UK). No differences were found in obtained values from either program; included images were exported from MetaEasy v1.0.4. Due to the wide paradigmatic variation and unknown effect of multiple-day stimulation protocols (eg – 10 consecutive days of anodal stimulation during a learning task), we only analyzed day 1 data from any study utilizing a multiple-day protocol.

Due to parametric variations within papers, we undertook two levels of analyses to balance the tradeoff between the maximum homogeneity achieved by including a smaller number of studies and our desire to also look for any more generalized effects seen across a broader sample of studies. Our primary analysis was limited to studies utilizing the same cognitive task with identical tDCS current densities and reference electrode locations. For this analysis, a fixed-effect (FE) model was utilized since, as the tDCS parameters and task were the same between studies, one would expect fairly homogenous results.

For our secondary analysis, all studies which utilized the same outcome measure were pooled and analyzed, regardless of current density and/or reference electrode location. This analysis included both the studies utilized in the first analysis and any additional study that used different current density and/or electrode montage. For this larger analysis, a DerSimonian-Laird (DL) mixed-effects model was selected since, as current density and reference electrode location parameters were variable, one would expect more heterogeneous results. As these parameters were chosen prior to analysis, homogeneity I^2 values will not be reported below.

Several studies in the literature have explored outcome measures included in the analysis below whilst targeting a neural region not replicated by a second group. Unfortunately, as these studies did not meet our inclusion criteria, we were unable to pool or meaningfully analyze them. For a list of these studies which have explored one of the outcome measures included in this paper but which targeted a different, non-replicated neural region, please see Supplementary Material (Table S2)

Results

Executive Functions: Primary Analysis

<INSERT TABLE 1>

<u>*Set Shifting*</u>*:* The directly-replicated anode/offline studies revealed a non-significant SMD effect size for the number of errors generated during task completion (Table1; Figure 1a). Only 1 study explored cathodal/offline stimulation [25]and only 1 study explored online tDCS on this task [29]; accordingly, no analysis was undertaken for these measures.

<u>*Stop Signal Task*</u>*:* The directly-replicated anode/offline studies revealed a non-significant SMD effect size for inhibitory reaction time to stop-signal stimuli (Table 1; Figure 1c). In addition, [27] and [28] further reported values for reaction time (RT) to non-stop-signal stimuli; analysis of this measure revealed a non-significant SMD effect size (Table 1; Figure 1b). Only 1 study explored the effect of anodal/online stimulation [30] and only 1 explored the effect of cathodal/offline stimulation on this task [31]; accordingly, no analysis was undertaken for these measures.

Executive Functions: Secondary Analysis

<INSERT TABLE 2>

Stop Signal Task: 6 non-directly comparable studies explored this task; 3 targeted M1 and 3 targeted pSMA. Analysis of the different locations revealed no significant SMD effect sizes for inhibitory reaction time to stop-signal stimuli (Table 2; Figure 1d,e).

Stroop Task: The non-directly comparable studies revealed no significant SMD effect sizes for task completion time (Table 2; Figure 1f,g). 2 studies explored the effects of cathodal/offline stimulation [35, 36]. As each came from the same research group, no analysis was undertaken. No studies have explored the effect of online stimulation on this measure.

<INSERT FIGURE 1>

Language: Primary Analysis

<INSERT TABLE 3>

Novel Language Learning Task: The directly-replicated anode/offline studies revealed a non-significant SMD effect size for task accuracy (Table 3; Figure 3a). Interestingly, although [41] noted an effect of stimulation on RT, [40] noted no effect of stimulation on RT: as this later group did not include any numeric data for this measure (only a verbal report), no analysis could be undertaken for this measure. No studies have explored the effect of online or cathodal stimulation on this task.

Picture Naming Task: 3 studies explored the effect of tDCS on this outcome measure by targeting the temporal lobes (2 from [49], 1 from [50]). Unfortunately, [49] only reported numerical data for accuracy (verbally noted no effect of stimulation on RT) whilst [50] only reported numerical data for RT (verbally noted no effect of stimulation on accuracy). Accordingly, no analysis was undertaken for these papers. In addition, 4 studies from 3 papers have explored the effect of tDCS on this outcome measure by targeting the left DLPFC [37, 42, 43]. Unfortunately, [42] and [43] both reported only numerical data for RT (though [42] verbally noted no effect of stimulation on accuracy) whilst [37] only reported numerical data for Accuracy. Accordingly, an analysis could only be undertaken exploring RT. Analysis of this measure revealed a non-significant SMD effect size (Table 3; Figure 3b). Although 4 studies

from 3 papers have explored the effect of anodal/online stimulation on this task, each targeted a different neural region; accordingly, no analysis could be undertaken. Finally, although 4 studies from 3 papers have explored the effect of cathodal stimulation on this task, each targeted a different neural region; accordingly, no analysis was undertaken.

Verbal Fluency: The directly-replicated anode/offline studies revealed a non-significant SMD effect size for word generation (Table 3; Figure 3d). Three comparable studies have explored the effect of anode/online stimulation on this task; however, as the current density and reference electrode location differed between each, we will explore this in the secondary analysis (below). No study has explored the effect of cathodal stimulation on this measure.

Language: Secondary Analysis

<INSERT TABLE 4>

Verbal Fluency: The non-directly comparable anode/online and anode/offline studies revealed no significant SMD effect size for word generation (Table 4; Figure 2c,d). No study explored the effect of cathodal stimulation on this measure.

<INSERT FIGURE 2>

Memory: Primary Analysis

<INSERT TABLE 5>

Digit Span Working Memory: The directly-replicated anode/offline studies revealed a non-significant SMD effect size for span length (Table 5; Figure 3a). No studies explored the effects of online or cathodal stimulation on this task.

Visual Working Memory: The directly-replicated anode/online studies revealed a non-significant SMD effect size for task accuracy or RT (Table 5; Figure 3g,h). Similarly, anode/offline studies revealed a non-significant SMD effect size for task accuracy (Table 5; Figure 3i). With regards to cathode/offline stimulation, analysis of the directly-replicated cathode/offline studies revealed a non-significant SMD effect size on task accuracy (Table 5; Figure 3j). No studies explored the effect of cathodal/online stimulation on this task. Finally, 2 studies have explored the effect of

anode/offline and cathode/offline stimulation on this task whilst targeting the cerebellum [66],[67]. Unfortunately, [66] only reported quantitative data for RT (verbally reported no effect on accuracy) whilst [67] only reported quantitative data for accuracy (verbally noted no effect on accuracy); accordingly, no analysis was undertaken.

N-Back Working Memory: As task difficulty increases with N, we decided to divide and analyze the remaining studies according to N (so that the effects of stimulation during a 1-back task do not skew effects during a 3-back task). Analyses of the directly-replicated studies revealed no significant SMD effect size for any measure (Table 5; Figure 4a,e,g).

Memory: Secondary Analysis

<INSERT TABLE 6>

Verbal Episodic Memory: The non-directly comparable anode and cathode studies during encoding revealed no significant SMD effect size for task accuracy (Table 6; Figure 3b,c). With regards to anode during *recognition*, [69] only reported numerical data for accuracy (verbally reported no effect on RT) whilst [82] only reported numerical data for RT (verbally reported no effect on accuracy); accordingly, no analysis was undertaken.

Visual Episodic Memory: The non-directly comparable anodal studies at each electrode location revealed no significant SMD effect size for task accuracy (Table 7c,d; Figure 3d,e). Similarly, the non-directly comparable cathodal studies revealed a non-significant SMD effect size for task accuracy (Table 6; Figure 3f).

Visual Working Memory: The non-directly comparable anode/offline studies revealed a non-significant SMD effect size for task accuracy (Table 6; Figure 3i). The non-directly comparable cathode/offline studies also revealed a non-significant SMD effect size on task accuracy (Table 6; Figure 3j). No studies explored the effect of cathodal/online stimulation on this task.

N-Back Working Memory: Again, as task difficulty increases with N, studies were divided according to N (so that the effects of stimulation during a 1-back task did not skew effects during a 3-back task). For a full breakdown, see table 6 and Figure 4. Analyses of the non-directly comparable studies revealed no significant SMD effect size for task accuracy, reaction time, or false alarm rate at any level.

Memory: Additional Pooled Analyses

As many of the aforementioned memory studies utilize tasks which explore a similar memory system (eg – working memory), we ran 8 additional analyses combining all studies exploring the same memory

system (regardless of specific task utilized). First, we pooled all anodal/online n-back working memory tasks, regardless of the 'n' value. Analysis revealed no significant SMD effect size for accuracy SMD [95%CI]= 0.19 [-0.13, 0.51], z=1.187, p=0.235: Figure 5a) or RT (SMD [95%CI]= -0.14 [-0.46, 0.18], z=-0.851, p=0.395: Figure 5b). Next, we pooled all anodal/offline n-back working memory tasks, regardless of the 'n' value. Again, analysis revealed no significant SMD effect size for accuracy (SMD [95%CI]= 0.29 [-0.02, 0.60], z=1.845, p=0.065: Figure 5e) or RT (SMD [95%CI]= -0.16 [-0.42, 0.09], z=-1.266, p=0.206: Figure 5f). Next, we pooled all anodal/online tasks exploring working memory (with a similar neural target). Again, analysis revealed no significant SMD effect size for accuracy (SMD [95%CI]= 0.29 [-0.04, 0.61], z=1.699, p=0.089: Figure 5c) or RT (SMD [95%CI]= -0.10 [-0.37, 0.17], z=-0.715, p=0.474: Figure 5d). Next, we pooled all anodal/offline tasks exploring working memory (with a similar neural target). Again, analysis revealed no significant SMD effect size for accuracy (SMD [95%CI]= 0.17 [-0.06, 0.4], z=1.438, p=0.151: Figure 5g). Finally, we pooled all anodal during encoding episodic memory tasks. Again, analysis revealed no significant SMD effect size for accuracy (SMD [95%CI]= 0.53 [-0.33, 1.38], z=1.211, p=0.226: Figure 5h). Complete analyses can be found in Supplemental Material: Table S1.

<INSERT FIGURE 3>

<INSERT FIGURE 4>

<INSERT FIGURE 5>

Miscellaneous: Primary Analysis

Due to a lack of directly replicable studies, no primary analysis could be undertaken on these measures.

Miscellaneous: Secondary Analysis

<INSERT TABLE 7>

<u>Mental Arithmetic</u>*:* The non-directly comparable anode/offline studies revealed a non-significant SMD effect size for task accuracy and RT (Table 7; Figure 6a,b). Only 1 study explored the effect of online stimulation on this task [93]; accordingly, no analysis was undertaken. No studies explored the effect of cathodal stimulation on this task.

<u>Picture Viewing/Rating</u>*:* The non-directly comparable anode/online studies revealed no significant SMD effect size for either negative or neutral valence image ratings (Table 7; Figure 7c,e,f,h). Similarly, the non-directly comparable cathode/online studies revealed no significant SMD effect size for either negative or neutral valence image ratings (Table 7; Figure 6d,g). Only

1 study explored the effect of offline stimulation on this task [94]; accordingly, no analysis was undertaken.

<u>Risk Taking</u>: The remaining non-comparable anode/online studies revealed no significant SMD effect size for task performance (Table 7; Figure 6i). Analysis of the non-comparable cathode/online studies revealed a non-significant SMD effect size for task performance (Table 7j; Figure 6j). Only 1 study explored the effect of offline stimulation on this task [95]; accordingly, no analysis was undertaken for this measure.

<u>Rumination Task</u>: The non-comparable anode/offline studies revealed a non-siignificant SMD effect size for rumination intensity (Table 7k; Table 6k). Only 1 study explored the effect of cathodal stimulation on this task [91]; accordingly, no analysis was undertaken. No studies explored the effect of online stimulation on this task.

<INSERT FIGURE 6>

Discussion

In this paper, we pooled and analyzed every cognitive outcome measure in the literature explored by at least two different research groups utilizing healthy adult populations, the same stimulation-to-task relationship, the same active electrode location, and comparing to a sham (control) condition. Of the 59 analyses undertaken, tDCS was not found to generate a significant effect on any. Taken together, the evidence does not support the assertion that a single-session of tDCS has a reliable effect on cognitive tasks in healthy adult populations.

A common criticism leveled at quantitative reviews concerns biased study selection: more specifically, through more- or less-stringent inclusion criteria, it is possible to skew analyses towards a positive result (for discussion, see: [96]). To address this issue, in this paper we undertook a two-tier analysis system. First we combined only those studies which demonstrated a direct replication of tDCS parametric values. The analysis was then expanded to combine all papers that targeted the same neural region and utilized the same task (regardless of current density and/or reference electrode location). Finally, in the case of memory, the analysis was further expanded to combine all papers that targeted the same neural region and utilized tasks thought to measure the same cognitive skill (eg – working memory). None of these analysis generated significant results. This suggests that the null results found in this paper are not likely the result of any specific sampling criteria (see limitations below).

One potential explanation for our findings rests in state-dependency: a concept which suggests that the effect an external stimulus exerts on the brain (and, by extension, cognition) is highly influenced by the state of the brain at the time of stimulus onset [97]. For instance, there is a large body of literature that demonstrates that the outcomes of single-, paired-, and repetitive-pulse TMS can be modulated according to the initial cortical activation state of the targeted neural region (for review: [98]). Similarly,

several studies have demonstrated that the effect of single-session tDCS on MEP amplitude can be negated following behavioral or cognitive priming [99,100] or reversed following neural priming using TMS [101]. Accordingly, it is likely that differential state-dependent effects between different studies included in this analysis influenced the null results obtained.

Luckily, state-dependent effects can be elucidated, controlled for, and possibly even leveraged to enhance the effects of tDCS; unfortunately, there is not enough comprehensive reporting in the literature to undertake such a synthesis at this point. It would be beneficial if future research included information concerning the time-of-day, day-of-week, duration, etc. of unique stimulation sessions and the satiation-levels, energy-levels, amount of sleep, etc. of individual participants. The inclusion of this information will not only allow for correlative and regression analyses to contextualize individual findings, but will also allow for more robust and meaningful quantitative pooling in the future.

Beyond methodological reporting, it is worth noting the relative lack of detailed data reporting in the literature. Though many studies explored for this analysis verbally reported a null finding on a particular measure, many did not offer quantitative or visual data amenable to pooling. This lack of data reporting has the undesirable effect of skewing quantitative analyses (such as this one). Accordingly, it would be beneficial if new studies included numerical data for all measures, even those with null-results: only by doing so can more meaningful analyses take place in the future.

Limitations

A major limitation of this analysis is the lack of comparable research available in the current tDCS literature. Of the 50 cognitive outcome measures replicated between two different research groups included in this paper, 35 include only 2 or 3 papers. Accordingly, these analyses must be interpreted with caution. It is worth noting, however, that of these 35 outcome measures, 25 include papers report opposing effect sizes. This means >70% of analyses which include only 2 or 3 papers contain at least 1 paper reporting enhancement and at least 1 paper reporting impairment following tDCS. As noted above, this may be due to varied state-dependency effects between different studies. Until more direct replication of older research is undertaken and more data are made available for pooling, it is difficult to conclude the true effect of this device.

Another limitation of this analysis concerns the population utilized. Although our results suggest tDCS has no reliable effect on cognitions in healthy adults, it remains to be seen whether or not tDCS can influence these measures in juvenile, elderly, or infirm populations. It is certainly possible that tDCS (known to be a relatively 'weak' form of modulation) simply does not work in a manner which can modulate a healthy, optimally performing brain (see: [102]). This does not preclude it from being able to modulate infirm, developing, or deteriorating brains. Additional analyses exploring the impact of tDCS in these populations are certainly warranted (examples of elderly population tDCS reviews: [103,104]; examples of infirm population tDCS meta-analyses: [105-107]).

This paper only explores cognitive measures undertaken during or following one session of tDCS. As noted in the results section, there are many studies which have utilized a multiple-day stimulation paradigm (eg - [39, 65, 79, 108]). It is wholly possible that several sessions of tDCS are required in order

for a reliable effect to be seen. In this instance, it has been argued tDCS impacts cognition via repeated exposure and, possibly, overnight consolidation (see: [109, 110]). Unfortunately, there simply are not enough comparable multiple-day stimulation studies conducted by two different research groups to assess if this is the case. As before, in order to determine the effect of repeated sessions of tDCS, more work directly replicating older research is required.

Conclusion

Taken together, we have found no evidence that single-session tDCS has a reliable effect on cognitions in healthy adult populations. When this is combined with our previous work which suggested tDCS does not have a reliable effect on neurophysiologic measures beyond MEP amplitude [1], it becomes difficult avoid questions of device efficacy. It is important to note, however, that these findings may be due to state dependency effects which, with elucidation, can be controlled for and leveraged. In addition, our findings do not preclude the possibility that tDCS has an effect on different populations (juvenile, elderly, infirm), when utilized multiple-times over several days or weeks, or on behavioral tasks. Nor does this preclude the possibility that tDCS could be effective if utilized in a novel fashion (hi-definition tDCS, spinal tDCS, pulsed current tDCS, etc.). Despite this, as this field moves forward, it will be important future studies include measures which directly replicate prior work, explore potential state-dependent effects within and between studies, and report quantitative data for all explored outcome measures (so that a more clear picture of the state of the field can be derived).

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Table Captions:

Table 1: *Studies and values for executive function task primary analyses*.

Table 2: *Studies and values for executive function task secondary analyses*.

Table 3: *Studies and values for language-based task primary analyses.*

Table 4: *Studies and values for executive function task secondary analyses*.

Table 5: *Studies and values for memory task primary analyses (N-Back excluded).*

Table 6: *Studies and values for memory task secondary analyses (N-Back excluded).*

Table 7: *Studies and values for miscellaneous task secondary analyses.*

Figure Captions:

<u>Figure 1:</u> Forest plots for both primary and secondary executive function analyses. (SMD = Standard Mean Difference; FE = Fixed Effect model for primary analyses; DL= DerSimonian-Laird mixed-effect model for secondary analyses; *Parentheses represent 95%CI).*

<u>Figure 2:</u> Forest plots for both primary and secondary language analyses. (SMD = Standard Mean Difference; FE = Fixed Effect model for primary analyses; DL= DerSimonian-Laird mixed-effect model for secondary analyses; *Parentheses represent 95%CI).*

<u>Figure 3:</u> Forest plots for both primary and secondary memory task analyses (n-back excluded). (SMD = Standard Mean Difference; FE = Fixed Effect model for primary analyses; DL= DerSimonian-Laird mixed-effect model for secondary analyses; *Parentheses represent 95%CI).*

<u>Figure 4:</u> Forest plots for both primary and secondary n-back task analyses. (SMD = Standard Mean Difference; FE = Fixed Effect model for primary analyses; DL= DerSimonian-Laird mixed-effect model for secondary analyses; *Parentheses represent 95%CI).*

<u>Figure 5:</u> Forest plots for each pooled-task memory analysis. (SMD = Standard Mean Difference; FE = Fixed Effect model for primary analyses; DL= DerSimonian-Laird mixed-effect model for secondary analyses; *Parentheses represent 95%CI).*

<u>Figure 6:</u> Forest plots for both secondary miscellaneous task analyses. (SMD = Standard Mean Difference; FE = Fixed Effect model for primary analyses; DL= DerSimonian-Laird mixed-effect model for secondary analyses; *Parentheses represent 95%CI).*

Table 1

Study	N	Active	Ref	Density (mA/cm2)	Task	SMD (95% CI)	Z Value	P Value
Set Shifting Tasks – Anode / Offline: **ERRORS**								
[25]	30	lDLPFC	rORBIT	0.0286	Cog	0.20 (-0.21, 0.61)	0.978	0.328
	30	lDLPFC	rORBIT	0.0286	Motor	-0.30 (-0.81, 0.21)	-1.150	0.250
[26]	46	lDLPFC	rORBIT	0.0286	Cog	0.08 (-0.42, 0.59)	0.325	0.745
				Fixed Effect Model		**0.03 (-0.27, 0.32)**	**0.207**	**0.836**
Stop Signal Task – Anode / Offline: **NO STOP REACTION TIME**								
[27]	11	rIFG	lORBIT	0.04	-	-0.10 (-0.93, 0.74)	-0.225	0.822
[28]	10a/ 12s	rIFG	lORBIT	0.0429	-	-0.91 (-1.79, -0.03)	-2.023	0.043
				Fixed Effect Model		**-0.48 (-1.09, 0.13)**	**-1.555**	**0.12**
Stop Signal Task – Anode / Offline: **STOP SIGNAL REACTION TIME (IFG)**								
[27]	11a/ 22s	rIFG	lORBIT	0.04	-	-0.21 (-0.93, 0.52)	-0.554	0.580
[28]	10a/ 12s	rIFG	lORBIT	0.0429	-	-0.13 (-0.97, 0.71)	-0.300	0.764
				Fixed Effect Model		**-0.17 (-0.72, 0.38)**	**-0.615**	**0.538**

General Notes: \Active = Acive electrode location; Ref = Reference electrode location; SMD = Standardized Mean Difference; A = Active; S = Sham; DLPFC = Dorsolateral prefrontal cortex; ORBIT = Orbitofrontal Location; IFG = Inferior frontal gyrus;
Set Shifting: Two studies from [25] were omitted due to targeting M1 (no comparable work elsewhere).
Stop Signal: All sham participants were pooled for [27].

Table 2

Study	N	Active	Ref	Density (mA/cm2)	Task	SMD (95% CI)	Z Value	P Value
Stop Signal Task – Anode / Offline: **STOP SIGNAL REACTION TIME (M1)**								
[32]	14a/ 28s	rM1	lCHK	0.0938	-	-0.13 (-0.77, 0.52)	-0.381	0.704
[30]	30	rM1	lORBIT	0.0286	-	-0.20 (-0.70, 0.31)	-0.753	0.451
[33]	40	rM1	lORBIT	0.0286	-	-0.30 (-0.75, 0.14)	-1.353	0.176
					DL Model	**-0.23 (-0.53, 0.07)**	**-1.521**	**0.128**
Stop Signal Task – Anode / Offline: **STOP SIGNAL REACTION TIME (pSMA)**								
[32]	14a/ 28s	rpSMA	lCHK	0.0938	-	-0.11 (-0.76, 0.53)	-0.347	0.728
[33]	40	rpSMA	lORBIT	0.0286	-	-1.30 (-1.78, -0.81)	-5.267	<0.001
[34]	18	rpSMA	lCHK	0.0938	-	-0.33 (-0.98, 0.33)	-0.973	0.331
					DL Model	**-0.60 (-1.38, 0.17)**	**-1.532**	**0.125**
Stroop Task – Anode / Offline: C**OMPLETION TIME (lDLPFC)**								
[35]	10	lDLPFC	rDLPFC	0.0571	-	1.31 (0.34, 2.27)	2.650	0.008
[36]	12	lDLPFC	rDLPFC	0.0571	-	0.87 (0.03, 1.70)	1.032	0.042
[37]	8	lDLPFC	rORBIT	0.0286	-	-0.54 (-1.54, 0.46)	-1.059	0.290
					DL Model	**0.56 (-1.60, 0.48)**	**1.056**	**0.291**
Stroop Task – Anode / Offline: C**OMPLETION TIME (rDLPFC)**								
[35]	10	rDLPFC	lDLPFC	0.0571	-	0.81 (-0.11, 1.72)	1.734	0.083
[36]	12	rDLPFC	lDLPFC	0.0571	-	0.58 (-0.24, 1.40)	1.387	0.165
[37]	8	rDLPFC	lORBIT	0.0286	-	-0.12 (-1.10, 0.86)	-0.236	0.831
					DL Model	**0.49 (-0.06, 0.98)**	**1.737**	**0.082**

General Notes: Active = Active electrode location; Ref = Reference electrode location; SMD = Standardized Mean Difference; A = Active; S = Sham; DLPFC = Dorsolateral prefrontal cortex; ORBIT = Orbitofrontal Location; IFG = Inferior frontal gyrus; CHK = Cheek; pSMA = Pre-supplementary motor area.
Stop Signal: All sham participants were pooled for [32]. [30] presented conflicting data regarding the number of participants: we used the N presented in the results section (n=30).
Stroop Task: [38] and [39] were omitted due to utilizing a 6-day and 5-day multiple day stimulation protocol, respectively (no day 1 data); though, each reported no effect of stimulation on the Stroop task.

Table 3:

Study	N	Active	Ref	Density (mA/cm2)	Task	SMD (95% CI)	Z Value	P Value
Novel Language Learning Task (Pictures to Words) – Anode / Offline: **ACCURACY**								
[40]	19	WNKE	rORBIT	0.0286	-	0.18 (-0.46, 0.82)	0.553	0.580
[41]	10	WNKE	rORBIT	0.0286	-	0.28 (-0.60, 1.16)	0.624	0.533
				Fixed Effect Model		**0.21 (-0.30, 0.73)**	**0.814**	**0.416**
Picture Naming Task – Anode / Offline: **RT**								
[42]	12	lDLPFC	rSHLD	0.0571	-	-0.09 (-0.89, 0.71)	-0.217	0.829
[43]	20	lDLPFC	rSHLD	0.0429	-	0.04 (-0.58, 0.66)	0.135	0.893
				Fixed Effect Model		**-0.01 (-0.50, 0.48)**	**-0.026**	**0.979**
Verbal Fluency Task – Anode / Offline: **NUMBER OF WORDS GENERATD**								
[44]	12	lDLPFC	rORBIT	0.0613	PHN	0.23 (-0.57, 1.4)	0.568	0.570
[45]	10	lDLPFC (+Broca)	rORBIT	0.0571	SMT	1.00 (0.07, 1.93)	2.110	0.035
	10	lDLPFC (+Broca)	rORBIT	0.0571	PHN	0.63 (-0.27, 1.53)	1.381	0.167
[46]	18	lDLPFC	rORBIT	0.0571	SMT	-0.23 (-0.89, 0.42)	-0.700	0.484
	18	lDLPFC (+Broca)	rORBIT	0.0571	SMT	0.43 (-0.29, 1.09)	1.283	0.199
	18	lDLPFC (+Broca)	rORBIT	0.0571	SMT	-0.27 (-0.93, 0.39)	-0.809	0.418
				Fixed Effect Model		**0.20 (-0.11, 0.50)**	**1.259**	**0.208**

General Notes: Active = Active electrode location; Ref = Reference electrode location; SMD = Standardized Mean Difference; A = Active; S = Sham; WNKE = Wernicke's area; RT = Reaction time; DLPFC = Dorsolateral prefrontal cortex; ORBIT = Orbitofrontal Location; PHN = Phonemic; SMT = Semantic;

Picture Naming: [37] was omitted from analysis as no quantitative RT data was reported.

Verbal Fluency: [47] was omitted from analysis as the young cohort only undertook sham stimulation. [48] did not supply quantitative data for the phonemic fluency task, though they verbally reported no effect of stimulation.

Table 4:

Study	N	Active	Ref	Density (mA/cm2)	Task	SMD (95% CI)	Z Value	P Value
Verbal Fluency Task – Anode / Online: **NUMBER OF WORDS GENERATD**								
[44]	18	lDLPFC	rORBIT	0.0613	PHN	-0.17 (-0.82, 0.49)	-0.494	0.621
[48]	12	lDLPFC	Cz	0.0370	SMT	0.49 (-0.32, 1.30)	1.185	0.236
[51]	20	lDLPFC (+Broca)	rORBIT	0.0286	SMT	0.73 (0.09, 1.38)	2.247	0.025
				DL Model		**0.35 (-0.22, 0.91)**	**1.210**	**0.226**
Verbal Fluency Task – Anode / Offline: **NUMBER OF WORDS GENERATD**								
[44]	12	lDLPFC	rORBIT	0.0613	PHN	0.23 (-0.57, 1.4)	0.568	0.570
[45]	10	lDLPFC (+Broca)	rORBIT	0.0571	SMT	1.00 (0.07, 1.93)	2.110	0.035
	10	lDLPFC (+Broca)	rORBIT	0.0571	PHN	0.63 (-0.27, 1.53)	1.381	0.167
[46]	18	lDLPFC	rORBIT	0.0571	SMT	-0.23 (-0.89, 0.42)	-0.700	0.484
	18	lDLPFC (+Broca)	rORBIT	0.0571	SMT	0.43 (-0.29, 1.09)	1.283	0.199
	18	lDLPFC (+Broca)	rORBIT	0.0571	SMT	-0.27 (-0.93, 0.39)	-0.809	0.418
[46]	18	lDLPFC (+Broca)	rDLPFC	0.0571	SMT	0.29 (-0.37, 0.95)	0.869	0.385
				DL Model		**0.23 (-0.09, 0.55)**	**1.406**	**0.160**

General Notes: Active = Active electrode location; Ref = Reference electrode location; SMD = Standardized Mean Difference; A = Active; S = Sham; WNKE = Wernicke's area; RT = Reaction time; DLPFC = Dorsolateral prefrontal cortex; ORBIT = Orbitofrontal Location; PHN = Phonemic; SMT = Semantic;
Verbal Fluency: [47] was omitted from analysis as the young cohort only undertook sham stimulation. [48]did not supply quantitative data for the phonemic fluency task, though they verbally reported no effect of stimulation. 1 study from [48] was omitted as it did not include numerical data (though they did verbally report no effect of stimulation on the total number of words generated).

Table 5:

Study	N	Active	Ref	Density (mA/cm2)	Task	SMD (95% CI)	Z Value	P Value
Digit Span Working Memory Task (forward & backward) – Anode / Offline: **SPAN**								
[52]	10	lDLPFC	rORBIT	0.0286	Forward	-3.22 (-1.21, 0.56)	-0.716	0.474
	10	lDLPFC	rORBIT	0.0286	Backward	0.483 (-0.41, 1.37)	1.065	0.287
	11a / 10s	lDLPFC	rORBIT	0.0286	Forward	0.065 (-0.79, 0.92)	0.148	0.882
	11a / 10s	lDLPFC	rORBIT	0.0286	Backward	0.018 (-0.84, 0.87)	0.040	0.968
[37]	8a / 16s	lDLPFC	rORBIT	0.0286	Forward	0.084 (-0.77, 0.93)	0.194	0.846
	8a / 16s	lDLPFC	rORBIT	0.0286	Backward	-0.25 (-1.10, 0.60)	-0.574	0.566
				Fixed Effect Model		**0.01 (-0.34, 0.36)**	**0.056**	**0.955**
Visual Working Memory – Anode / Online: **ACCURACY**								
[53]	12	lDLPFC	rORBIT	0.0286	STRNBRG	0.000 (-1.62, 0.86)	0.000	1.000
[54]	14	lDLPFC	rORBIT	0.0286	STRNBRG	1.14 (0.34, 1.94)	2.803	0.005
				Fixed Effect Model		**0.57 (-0.55, 1.70)**	**1.000**	**0.317**
Visual Working Memory – Anode / Online: **RT**								
[53]	12	lDLPFC	rORBIT	0.0286	STRNBRG	-0.07 (-0.87, 0.73)	-0.177	0.859
[54]	14	lDLPFC	rORBIT	0.0286	STRNBRG	0.04 (-0.70, 0.78)	0.107	0.915
				Fixed Effect Model		**-0.01 (-0.55, 0.53)**	**-0.042**	**0.966**
Visual Working Memory – Anode / Offline: **ACCURACY**								
[55]	11	rPPC	lCHK	0.0429		-0.07 (-0.90, 0.77)	-0.153	0.878
	11	rPPC	lCHK	0.0429		-0.50 (-1.35, 0.35)	-1.160	0.246
[56]	20	rPPC	lCHK	0.0429		-0.42 (-1.04, 0.21)	-1.298	0.194
[57]	9	rPPC	lCHK	0.0938		1.06 (0.07, 2.04)	2.099	0.036
	20	rPPC	lCHK	0.0938		0.14 (-0.48, 0.76)	0.451	0.652
[58]	20	rPPC	lCHK	0.0938		0.14 (-0.48, 0.76)	0.451	0.652
				Fixed Effect Model		**-0.00 (-0.30, 0.29)**	**-0.012**	**0.991**
Visual Working Memory – Cathode / Offline: **ACCURACY**								
[55]	11	rPPC	lCHK	0.0429		-0.09 (-0.93, 0.75)	-0.211	0.833
	11	rPPC	lCHK	0.0429		-0.66 (-1.52, 0.20)	-1.504	0.133
[56]	20	rPPC	lCHK	0.0429		0.18 (-0.44, 0.80)	0.569	0.569
[59]	24	rPPC	lCHK	0.0429		0.43 (-0.14, 1.00)	1.468	0.142
				Fixed Effect Model		**0.09 (-0.26, 0.43)**	**0.509**	**0.611**
Two-Back Working Memory Task – Anode / Offline: **RT**								
[53]	12	lDLPFC	rORBIT	0.02857	2-Back	-0.45 (-1.26, 0.36)	-1.095	0.274
[60]	18	lDLPFC	rORBIT	0.02857	2-Back	-0.29 (-0.95, 0.37)	-0.868	0.385
				Fixed Effect Model		**-0.39 (-0.90, 0.12)**	**-1.364**	**0.173**
[61]	10	lDLPFC	rORBIT	0.05714	2-Back	-0.33 (-1.22, 0.55)	-0.741	0.459
[60]	18	lDLPFC	rORBIT	0.05714	2-Back	-0.02 (-0.68, 0.63)	-0.073	0.942
				Fixed Effect Model		**-0.13 (-0.66, 0.40)**	**-0.499**	**0.617**
Three-Back Working Memory Task – Anode / Online: **ACCURACY**								
[62]	15	lDLPFC	rORBIT	0.02857	3-Back	0.31 (-0.41, 1.03)	0.855	0.393
[63]	12	lDLPFC	rORBIT	0.02857	3-Back	0.05 (-0.71, 0.81)	0.125	0.901

				Fixed Effect Model		**0.19 (-0.33, 0.71)**	**0.706**	**0.480**
[64]	15	lDLPFC	rORBIT	0.04	3-Back	0.36 (-0.37, 1.08)	0.966	0.334
[63]	12	lDLPFC	rORBIT	0.05714	3-Back	-0.05 (-0.81, 0.71)	-0.128	0.898
				Fixed Effect Model		**0.16 (-0.36, 0.69)**	**0.612**	**0.541**
Three-Back Working Memory Task – Anode / Online: **RT**								
[62]	15	lDLPFC	rORBIT	0.02857	3-Back	0.00 (-0.71, 0.72)	0.011	0.991
[63]	12	lDLPFC	rORBIT	0.02857	3-Back	-0.30 (-1.11, 0.50)	-0.736	0.462
				Fixed Effect Model		**-0.13 (-0.67, 0.40)**	**-0.481**	**0.631**
[64]	15	lDLPFC	rORBIT	0.04	3-Back	0.01 (-0.70, 0.73)	0.032	0.974
[63]	12	lDLPFC	rORBIT	0.05714	3-Back	-0.32 (-1.13, 0.48)	-0.781	0.435
				Fixed Effect Model		**-0.14 (-0.67, 0.40)**	**-0.495**	**0.621**

General Notes: Active = Active electrode location; Ref = Reference electrode location; SMD = Standardized Mean Difference; A = Active; S = Sham; DLPFC = Dorsolateral prefrontal cortex; ORBIT = Orbitofrontal Location; DELT = Deltoid Muscle; ATL = Anterior Temporal lobe; SMG = Supramarginal Gyrus; STRNBRG = Sternberg working memory task; PPC = Posterior Parietal Cortex; CHK = Cheek; IPS = Inferior Parietal Sulcus; RT = Reaction time.
Digit Span: Two sham groups were pooled in Jeon 2013.
Visual Working Memory: Values collapsed across hemifields and array sizes. Values for the second study from Tseng 2012 and Hsu 2014 are collapsed across all participants (data appear to be identical for these studies). Bolognini 2010 was omitted from analysis as they did not report any data for accuracy. Tanoue 2013 utilized a cueing paradigm – only the data from the cue-less trials was utilized.
N-Back Tasks: Data for [64] and [63] were collapsed across two online blocks. [60] was omitted from both accuracy and RT analysis due to no discernable quantitative data being made available. A description in the text noted no effect of either low- or high-density stimulation on accuracy or RT. [52] was omitted from analysis due to not reporting quantitative data. [65] was omitted due to utilizing a 10-day stimulation protocol (no day 1 data). 1 study from [60] was omitted due to not reporting quantitative data (though they verbally reported no effect of stimulation on accuracy or RT data during a 3-back task, and no effect on accuracy during a 2-back task).

Table 6:

Study	N	Active	Ref	Density (mA/cm2)	Task	SMD (95% CI)	Z Value	P Value
Verbal Episodic Memory Task: Recognition (stim during encoding) – Anode: **ACCURACY**								
[68]	18	lDLPFC	rORBIT	0.0286	Errorless Learning	-0.17 (-0.82, 0.49)	-0.502	0.616
	18	lDLPFC	rORBIT	0.0286	Errorful Learning	0.268 (-0.39, 0.92)	0.800	0.424
[69]	16	lDLPFC	rORBIT	0.0816	-	3.00 (1.99, 4.01)	5.821	<0.001
					DL Model	**1.03 (-0.87, 2.94)**	**1.188**	**0.235**
Verbal Episodic Memory Task: Recognition (stim during encoding) – Cathode: **ACCURACY**								
[68]	18	lDLPFC	rORBIT	0.0286	Errorless Learning	0.120 (-0.53, 0.77)	0.360	0.719
	18	lDLPFC	rORBIT	0.0286	Errorful Learning	-0.31 (-0.97, 0.35)	-0.932	0.351
[69]	16	lDLPFC	rORBIT	0.0816	-	-2.35 (-3.25, -1.45)	-5.117	<0.001
					DL Model	**-0.81 (-2.14, 0.51)**	**-1.201**	**0.230**
Visual Episodic Memory Task: Recognition (stim during encoding) – Anode: **ACCURACY (DLPFC)**								
[70]	15	lDLPFC	rORBIT	0.0286	Cued Learning	0.037 (-0.45, 0.53)	0.146	0.884
[71]	24a / 48s	lDLPFC	rDELT	0.0571	-	-0.14 (-0.86, 0.58)	-0.385	0.700
					DL Model	**-0.02 (-0.42, 0.39)**	**-0.096**	**0.923**
Visual Episodic Memory Task: Recognition (stim during encoding) – Anode: **ACCURACY (TEMP)**								
[72]	12	lATL	rATL	0.0571	-	-0.11 (-0.91, 0.70)	-0.257	0.797
[73]	12	lSMG	rORBIT	0.08	-	-0.15 (-0.95, 0.65)	-0.365	0.715
					DL Model	**-0.13 (-0.69, 0.44)**	**-0.440**	**0.660**
Visual Episodic Memory Task: Recognition (stim during encoding) – Cathode: **ACCURACY (TEMP)**								
[72]	12	lATL	rATL	0.0571	-	1.10 (0.24, 1.96)	2.509	0.012
[73]	12	lSMG	rORBIT	0.08	-	-0.08 (-0.88, 0.72)	-0.198	0.843
					DL Model	**0.50 (-0.66, 1.65)**	**0.845**	**0.398**
Visual Working Memory – Anode / Offline: **ACCURACY**								
[55]	11	rPPC	lCHK	0.0429		-0.07 (-0.90, 0.77)	-0.153	0.878
	11	rPPC	lCHK	0.0429		-0.50 (-1.35, 0.35)	-1.160	0.246
[56]	20	rPPC	lCHK	0.0429		-0.42 (-1.04, 0.21)	-1.298	0.194
[57]	9	rPPC	lCHK	0.0938		1.06 (0.07, 2.04)	2.099	0.036
	20	rPPC	lCHK	0.0938		0.14 (-0.48, 0.76)	0.451	0.652
[58]	20	rPPC	lCHK	0.0938		0.14 (-0.48, 0.76)	0.451	0.652
[74]	12	rPPC	lPPC	0.0286		-0.42 (-1.22, 0.39)	-1.005	0.315
[75]	20	rIPS	lORBIT	0.0286		-0.16 (-0.78, 0.46)	-0.495	0.620
					DL Model	**-0.06 (-0.35, 0.22)**	**-0.435**	**0.664**
Visual Working Memory – Cathode / Offline: **ACCURACY**								
[55]	11	rPPC	lCHK	0.0429		-0.09 (-0.93, 0.75)	-0.211	0.833
	11	rPPC	lCHK	0.0429		-0.66 (-1.52, 0.20)	-1.504	0.133
[56]	20	rPPC	lCHK	0.0429		0.18 (-0.44, 0.80)	0.569	0.569

[59]	24	rPPC	lCHK	0.0429		0.43 (-0.14, 1.00)	1.468	0.142
[74]	12	rPPC	lPPC	0.0286		-0.08 (-0.88, 0.72)	-0.200	0.842
[75]	20	rIPS	lORBIT	0.0286		-0.14 (-0.76, 0.48)	-0.448	0.654
	20	rIPS	lORBIT	0.0571		0.09 (-0.53, 0.71)	0.293	0.769
					DL Model	**0.03 (-0.22, 0.29)**	**0.251**	**0.802**
One-Back Working Memory Task – Anode / Offline: **ACCURACY**								
[61]	10	lDLPFC	rORBIT	0.05714	1-Back	-0.08 (-0.96, 0.80)	-0.184	0.854
[53]	12	lDLPFC	rORBIT	0.02857	1-Back	0.50 (-0.31, 1.31)	1.206	0.228
					DL Model	**0.23 (-0.37, 0.83)**	**0.760**	**0.447**
One-Back Working Memory Task – Anode / Offline: **RT**								
[61]	10	lDLPFC	rORBIT	0.05714	1-Back	0.55 (-0.34, 1.44)	1.208	0.227
[53]	12	lDLPFC	rORBIT	0.02857	1-Back	-0.26 (-1.07, 0.54)	-0.638	0.524
					DL Model	**0.12 (-0.67, 0.91)**	**0.296**	**0.767**
Two-Back Working Memory Task – Anode / Offline: **ACCURACY**								
[61]	10	lDLPFC	rORBIT	0.05714	2-Back	0.46 (-0.43, 1.35)	1.019	0.308
[53]	12	lDLPFC	rORBIT	0.02857	2-Back	-0.40 (-1.21, 0.41)	-0.970	0.332
[76]	16	lDLPFC	rMAST	0.02857	2-Back	0.39 (-0.36, 1.04)	0.949	0.343
					DL Model	**0.14 (-0.38, 0.65)**	**0.515**	**0.606**
Two-Back Working Memory Task – Anode / Offline: **RT**								
[53]	12	lDLPFC	rORBIT	0.02857	2-Back	-0.45 (-1.26, 0.36)	-1.095	0.274
[60]	18	lDLPFC	rORBIT	0.02857	2-Back	-0.29 (-0.95, 0.37)	-0.868	0.385
[61]	10	lDLPFC	rORBIT	0.05714	2-Back	-0.33 (-1.22, 0.55)	-0.741	0.459
[60]	18	lDLPFC	rORBIT	0.05714	2-Back	-0.02 (-0.68, 0.63)	-0.073	0.942
[76]	16	lDLPFC	rMAST	0.02857	2-Back	0.46 (-0.24, 1.17)	1.293	0.196
					DL Model	**-0.10 (-0.42, 0.23)**	**-0.579**	**0.563**
Three-Back Working Memory Task – Anode / Online: **ACCURACY**								
[62]	15	lDLPFC	rORBIT	0.02857	3-Back	0.31 (-0.41, 1.03)	0.855	0.393
[63]	12	lDLPFC	rORBIT	0.02857	3-Back	0.05 (-0.71, 0.81)	0.125	0.901
[64]	15	lDLPFC	rORBIT	0.04	3-Back	0.36 (-0.37, 1.08)	0.966	0.334
[63]	12	lDLPFC	rORBIT	0.05714	3-Back	-0.05 (-0.81, 0.71)	-0.128	0.898
[77]	9a 10	lDLPFC	rCHK	0.02857	3-Back	0.97 (0.01, 1.92)	1.988	0.047
					DL Model	**0.28 (-0.07, 0.62)**	**1.589**	**0.112**
Three-Back Working Memory Task – Anode / Online: **FA**								
[62]	15	lDLPFC	rORBIT	0.02857	3-Back	-0.40 (-1.13, 0.32)	-1.095	0.273
[64]	15	lDLPFC	rORBIT	0.04	3-Back	0.00 (-0.72, 0.72)	0.000	1.000
[77]	9a 10	lDLPFC	rCHK	0.02857	3-Back	-1.16 (-2.14, -0.19)	-2.339	0.019
					DL Model	**-0.45 (-1.06, 0.16)**	**-1.446**	**0.148**
Three-Back Working Memory Task – Anode / Online: **RT**								
[62]	15	lDLPFC	rORBIT	0.02857	3-Back	0.00 (-0.71, 0.72)	0.011	0.991
[63]	12	lDLPFC	rORBIT	0.02857	3-Back	-0.30 (-1.11, 0.50)	-0.736	0.462
[64]	15	lDLPFC	rORBIT	0.04	3-Back	0.01 (-0.70, 0.73)	0.032	0.974
[63]	12	lDLPFC	rORBIT	0.05714	3-Back	-0.32 (-1.13, 0.48)	-0.781	0.435
[77]	9a 10	lDLPFC	rCHK	0.02857	3-Back	0.02 (-0.88, 0.92)	0.037	0.971

				DL Model		**-0.11 (-0.46, 0.23)**	**-0.648**	**0.517**
Three-Back Working Memory Task – Anode / Offline: **ACCURACY**								
[64]	15	lDLPFC	rORBIT	0.04	3-Back	0.84 (0.10, 1.59)	2.214	0.027
[77]	9a 10	lDLPFC	rCHK	0.02857	3-Back	0.22 (-0.69, 1.12)	0.466	0.641
				DL Model		**0.58 (-0.03, 1.19)**	**1.879**	**0.060**
Three-Back Working Memory Task – Anode / Offline: **FA**								
[64]	15	lDLPFC	rORBIT	0.04	3-Back	0.00 (-0.72, 0.72)	0.000	1.000
[77]	9a 10	lDLPFC	rCHK	0.02857	3-Back	-0.62 (-1.54, 0.31)	-1.312	0.190
				DL Model		**-0.24 (-0.83, 0.35)**	**-0.804**	**0.421**
Three-Back Working Memory Task – Anode / Offline: **RT**								
[64]	15	lDLPFC	rORBIT	0.04	3-Back	-0.01 (-0.72, 0.71)	-0.015	0.988
[77]	9a 10	lDLPFC	rCHK	0.02857	3-Back	-0.02 (-0.92, 0.88)	-0.047	0.962
				DL Model		**-0.01 (-0.57, 0.55)**	**-0.041**	**0.967**

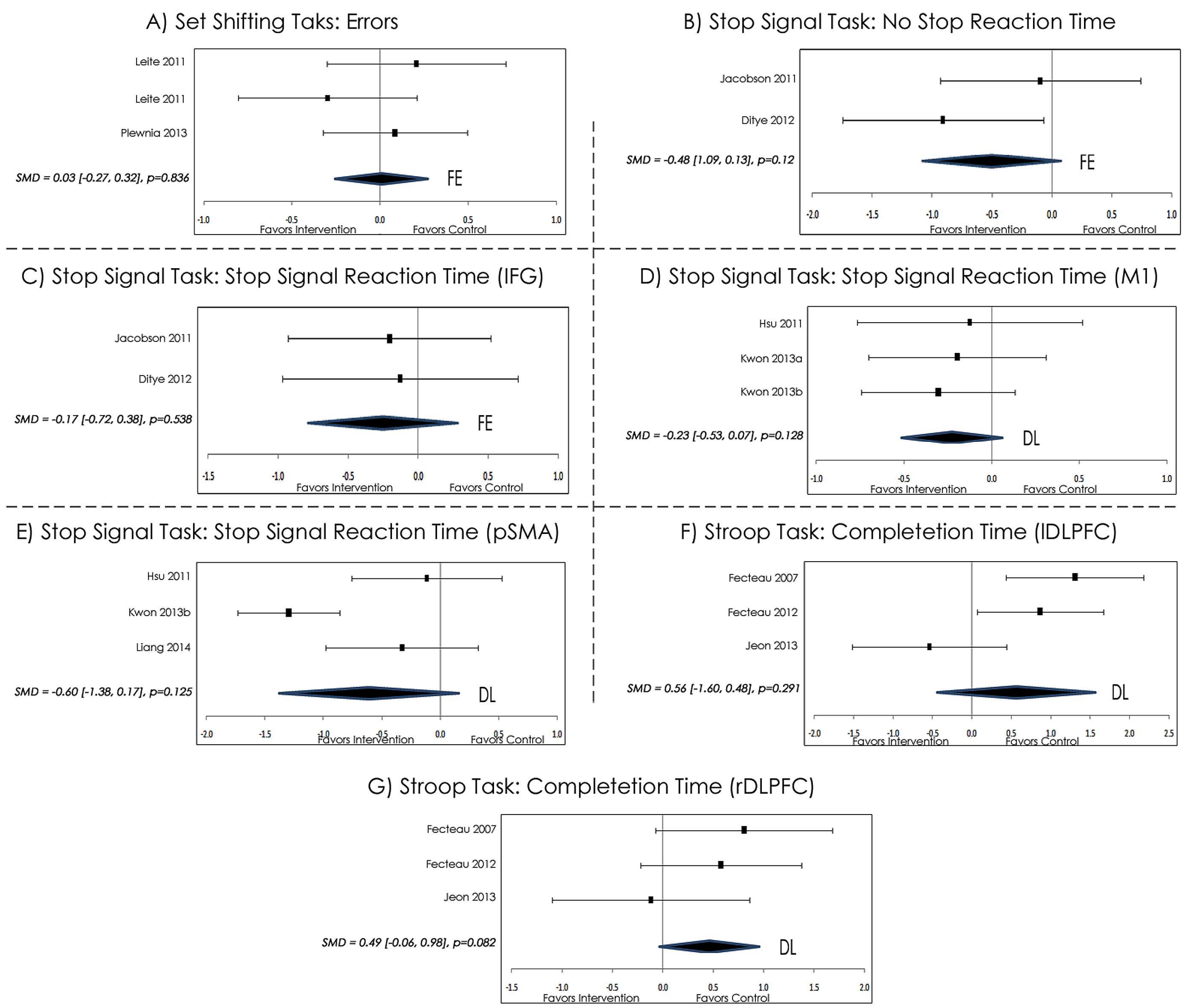
General Notes: Active = Active electrode location; Ref = Reference electrode location; SMD = Standardized Mean Difference; A = Active; S = Sham; DLPFC = Dorsolateral prefrontal cortex; ORBIT = Orbitofrontal Location; DELT = Deltoid Muscle; ATL = Anterior Temporal lobe; SMG = Supramarginal Gyrus; STRNBRG = Sternberg working memory task; PPC = Posterior Parietal Cortex; CHK = Cheek; IPS = Inferior Parietal Sulcus; RT = Reaction time; MAST = Mastoid; FA = False alarms.
Verbal Episodic Memory: [68] presented only values pooled between online and offline measures. Two studies from [69] were omitted: one for targeting M1, one for generating stimulation during recognition (no comparable work elsewhere). [78] was omitted due to using very-short duration (1.6s) stimulation during recognition only (no comparable work elsewhere). [79] was omitted due to utilizing a 5-day stimulation protocol (no day 1 data).
Visual Episodic Memory: Two studies from [54] were omitted as they utilized an interference paradigm in the Sternberg task (no comparable work elsewhere). [80] was omitted due to using a 10-day stimulation paradigm (no day 1 data). Values were collapsed across array sizes.
Visual Working Memory: Values collapsed across hemifields and array sizes. Values for the second study from [57] and [58] are collapsed across all participants (data appear to be identical for these studies). [81] was omitted from analysis as they did not report any data for accuracy. [59] utilized a cueing paradigm – only the data from the cue-less trials was utilized.
Two-Back: [60] was omitted from the accuracy analysis due to no discernable quantitative data being made available. A description in the text noted no effect of either low- or high-density stimulation on accuracy.
Three-Back: Only data from day one of [77] was used for analysis. Data for [64] and [63] were collapsed across two online blocks. [60] was omitted from both accuracy and RT analysis due to no discernable quantitative data being made available. A description in the text noted no effect of either low- or high-density stimulation on accuracy or RT.

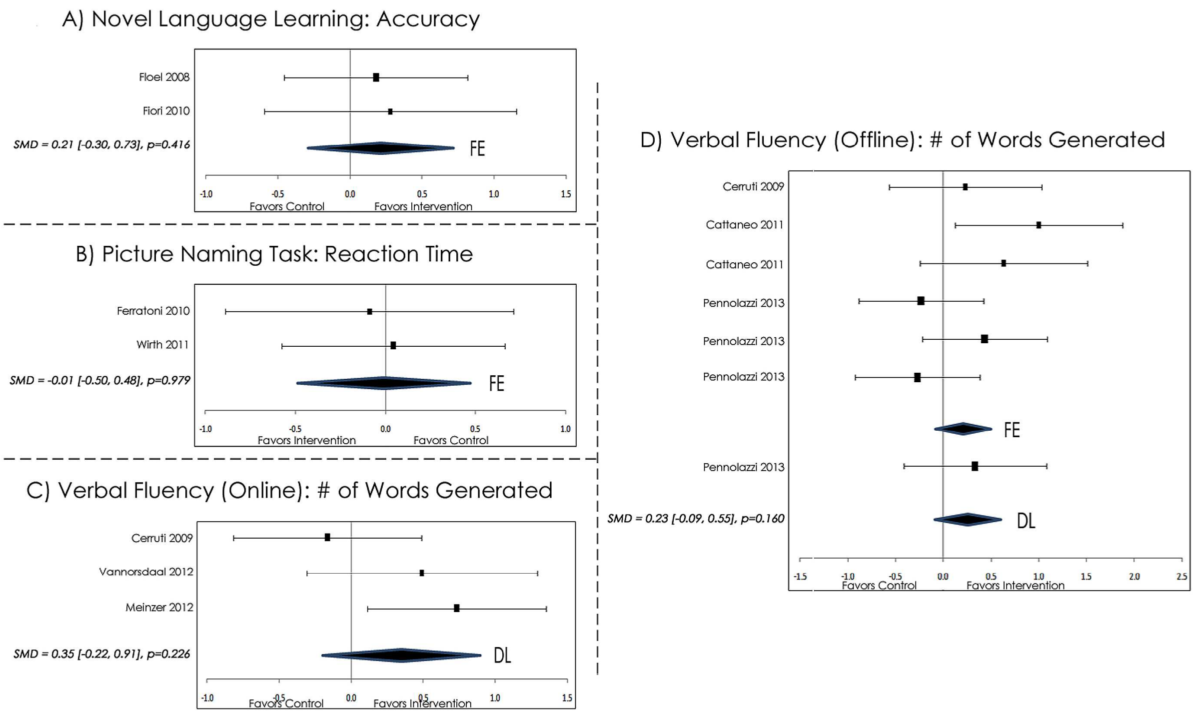
Table 7:

Study	N	Active	Ref	Density (mA/cm2)	Task	SMD (95% CI)	Z Value	P Value
Mental Arithmetic Ability – Anode / Offline: **ACCURACY**								
[83]	10	rPAR	lORBIT	0.0571	MULT	0.18 (-0.70, 1.06)	0.3989	0.691
[84]	16	rPAR	lORBIT	0.0286	SUB	-0.23 (-0.93, 0.47)	-0.647	0.518
					DL Model	**-0.07 (-0.62, 0.47)**	**-0.261**	**0.794**
Mental Arithmetic Ability – Anode / Offline: **TIME TO SOLVE**								
[83]	10	rPAR	lORBIT	0.0571	MULT	-0.18 (-1.06, 0.70)	-0.398	0.691
[84]	16	rPAR	lORBIT	0.0286	SUB	-0.33 (-1.03, 0.37)	-0.925	0.355
					DL Model	**-0.27 (-0.82, 0.28)**	**-0.971**	**0.331**
Negative Valence Picture Viewing – Anode / Online: **NEGATIVITY RATING (lDLPFC)**								
[85]	23	lDLPFC	rORBIT	0.0571	-	-0.26 (-0.84, 0.32)	-0.884	0.377
[86]	16a/ 32s	lDLPFC	rM1	0.0286	-	-0.37 (-0.97, 0.24)	-1.192	0.233
[87]	20	lDLPFC	rDLPFC	0.0429	-	0.14 (-0.48, 0.76)	0.438	0.661
					DL Model	**-0.17 (-0.52, 0.18)**	**-0.968**	**0.333**
Negative Valence Picture Viewing – Cathode / Online: **NEGATIVITY RATING (lDLPFC)**								
[86]	16a/ 32s	lDLPFC	rM1	0.0286	-	-0.25 (-0.86, 0.35)	-0.826	0.409
[87]	20	lDLPFC	rDLPFC	0.0429	-	0.33 (-0.30, 0.95)	1.029	0.304
					DL Model	**0.03 (-0.54, 0.60)**	**0.106**	**0.915**
Negative Valence Picture Viewing – Anode / Online: **NEGATIVITY RATING (rDLPFC)**								
[87]	20	rDLPFC	lDLPFC	0.0429	-	0.33 (-0.30, 0.95)	1.029	0.304
[88]	23a/ 25s	rDLPFC	lORBIT	0.0429	-	-0.70 (-1.28, -0.12)	-2.347	0.019
					DL Model	**-0.19 (-1.20, 0.81)**	**-0.374**	**0.709**
Neutral Valence Picture Viewing – Anode / Online: **NEGATIVITY RATING (lDLPFC)**								
[86]	16a/ 32s	lDLPFC	rM1	0.0286	-	-0.12 (-0.72, 0.48)	-0.389	0.697
[87]	20	lDLPFC	rDLPFC	0.0429	-	0.15 (-0.47, 0.77)	0.476	0.634
					DL Model	**0.01 (-0.42, 0.45)**	**0.054**	**0.957**
Neutral Valence Picture Viewing – Cathode / Online: **NEGATIVITY RATING (lDLPFC)**								
[86]	16a/ 32s	lDLPFC	rM1	0.0286	-	0.42 (-0.19, 1.02)	1.336	0.181
[87]	20	lDLPFC	rDLPFC	0.0429	-	0.33 (-0.30, 0.95)	1.026	0.305
					DL Model	**0.37 (-0.06, 0.81)**	**1.673**	**0.094**
Neutral Valence Picture Viewing – Anode / Online: **NEGATIVITY RATING (rDLPFC)**								
[87]	20	rDLPFC	lDLPFC	0.0429	-	0.33 (-0.30, 0.95)	1.026	0.305
[88]	23a/ 25s	rDLPFC	lORBIT	0.0429	-	-0.05 (-0.62, 0.52)	-0.175	0.861
					DL Model	**0.12 (-0.30, 0.54)**	**0.560**	**0.575**
Gambling-Based Risk Taking – Anode / Online: **RISK PROPENSITY**								
[35]	10	lDLPFC	rDLPFC	0.0571	MB	-2.95 (-4.22, -1.69)	-4.568	<0.001

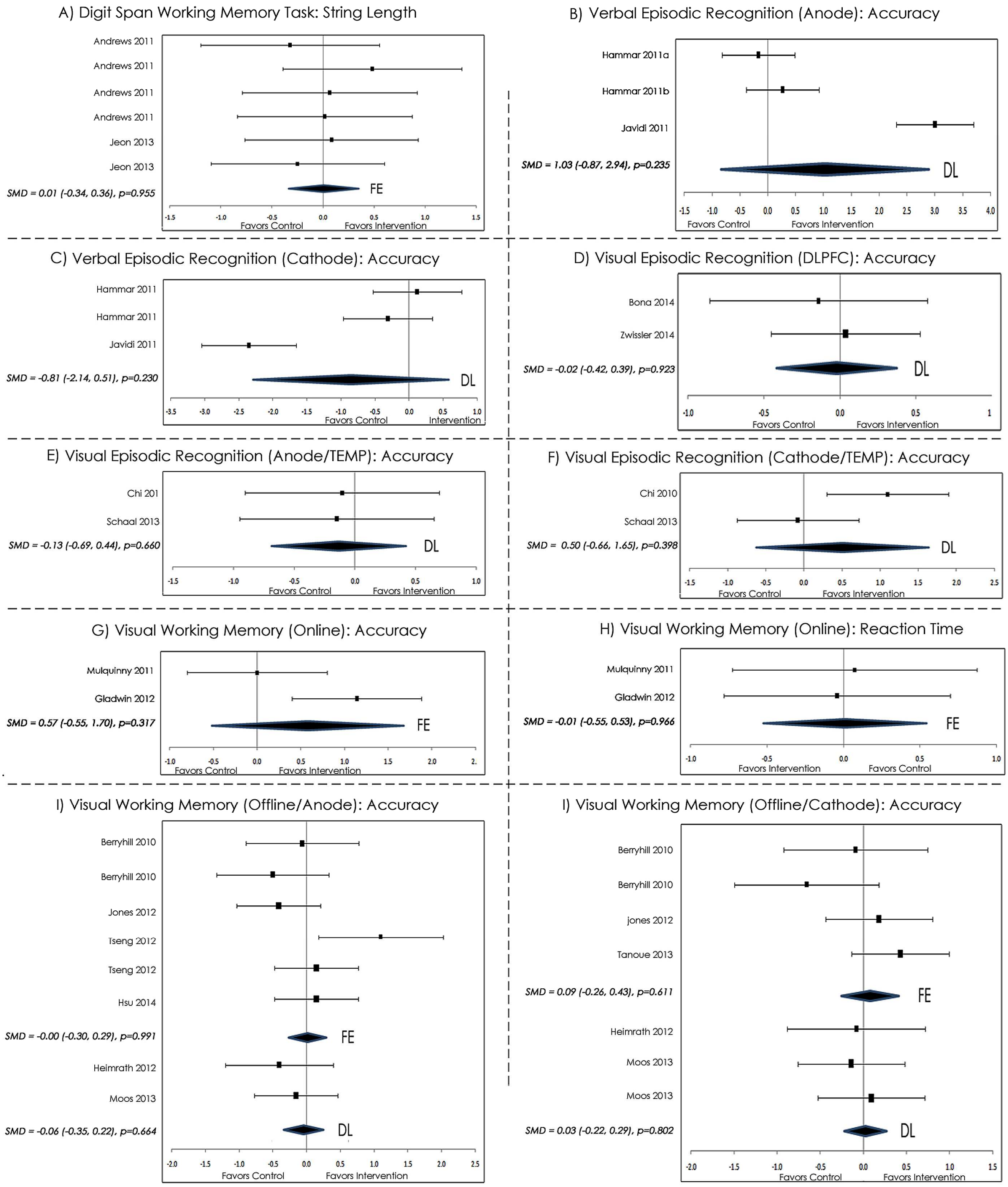
[89]	12	lDLPFC	rDLPFC	0.0571	GT	0.58 (-0.24, 1.39)	1.385	0.166
[90]	16	lDLPFC	rDLPFC	?	GT	0.14 (-0.55, 0.84)	0.404	0.687
					DL Model	**-0.67 (-2.39, 1.06)**	**-0.754**	**0.451**
Gambling-Based Risk Taking – Cathode / Online: **RISK PROPENSITY**								
[35]	10	lDLPFC	rDLPFC	0.0571	MB	-3.38 (-4.74, -2.01)	-4.848	<0.001
[89]	12	lDLPFC	rDLPFC	0.0571	GT	-1.92 (-2.89, -0.96)	-3.895	<0.001
[90]	16	lDLPFC	rDLPFC	?	GT	0.00 (-0.69, 0.69)	0.000	1.000
					DL Model	**-1.70 (-3.61, 0.22)**	**-1.738**	**0.082**
Rumination Task – Anode / Offline: **SELF-RUMINATION INTENSITY**								
[91]	29a/ 33s	lDLPFC	rDLPFC	0.0571	-	0.07 (-0.43, 0.57)	0.282	0.778
[92]	32	lDLPFC	rORBIT	0.0571	-	-0.09 (-0.58, 0.40)	-0.364	0.716
					DL Model	**-0.01 (-0.36, 0.34)**	**-0.063**	**0.950**

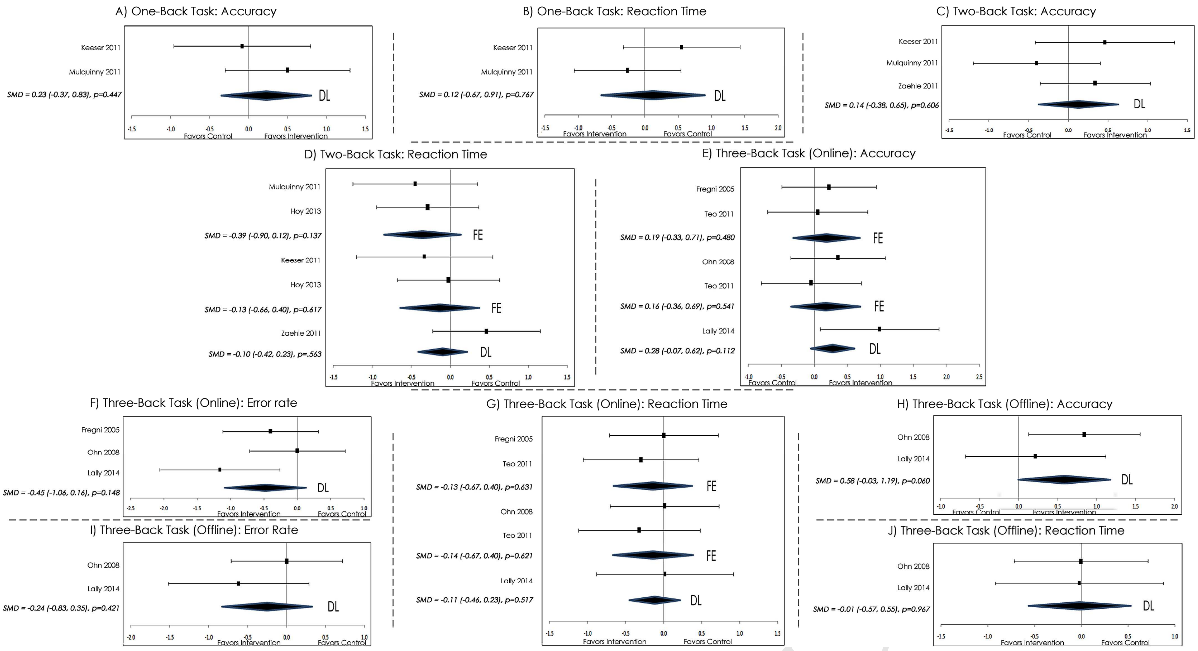
General Notes: Active = Active electrode location; Ref = Reference electrode location; SMD = Standardized Mean Difference; A = Active; S = Sham; PAR = Parietal cortex; MULT = Multiplication task; SUB = Subtraction task; RT = Reaction time; DLPFC = Dorsolateral prefrontal cortex; MB = Monetary balloon analogue risk task; GT = Gambling Task;
Mental Math: The value reported by [83] combined both RT and Accuracy – accordingly, the same value was used for both the accuracy and RT analyses. As the value represents an improvement following stimulation, it is represented as positive (higher score) in the accuracy analysis and negative (faster response) in the RT analysis.
Picture Viewing: All sham participants were pooled for [86]. Two studies from [85] were omitted from analysis due to targeting M1 and V1, respectively (no comparable work elsewhere). Only the 'maintain' condition from [88]was analyzed.
Risk Taking: Due to the unknown current density of [90], we analyzed using a DL model. Two studies from [35] were omitted for not including a sham condition.


A) Set Shifting Taks: Errors
Leite 2011
Leite 2011
Plewnia 2013
SMD = 0.03 [-0.27, 0.32], p=0.836
FE
Favors Intervention
Favors Control
B) Stop Signal Task: No Stop Reaction Time
Jacobson 2011
Ditye 2012
SMD = -0.48 [1.09, 0.13], p=0.12
FE
Favors Intervention
Favors Control
C) Stop Signal Task: Stop Signal Reaction Time (IFG)
Jacobson 2011
Ditye 2012
SMD = -0.17 [-0.72, 0.38], p=0.538
FE
Favors Intervention
Favors Control
D) Stop Signal Task: Stop Signal Reaction Time (M1)
Hsu 2011
Kwon 2013a
Kwon 2013b
SMD = -0.23 [-0.53, 0.07], p=0.128
DL
Favors Intervention
Favors Control
E) Stop Signal Task: Stop Signal Reaction Time (pSMA)
Hsu 2011
Kwon 2013b
Liang 2014
SMD = -0.60 [-1.38, 0.17], p=0.125
DL
Favors Intervention
Favors Control
F) Stroop Task: Completetion Time (lDLPFC)
Fecteau 2007
Fecteau 2012
Jeon 2013
SMD = 0.56 [-1.60, 0.48], p=0.291
DL
Favors Intervention
Favors Control
G) Stroop Task: Completetion Time (rDLPFC)
Fecteau 2007
Fecteau 2012
Jeon 2013
SMD = 0.49 [-0.06, 0.98], p=0.082
DL
Favors Intervention
Favors Control

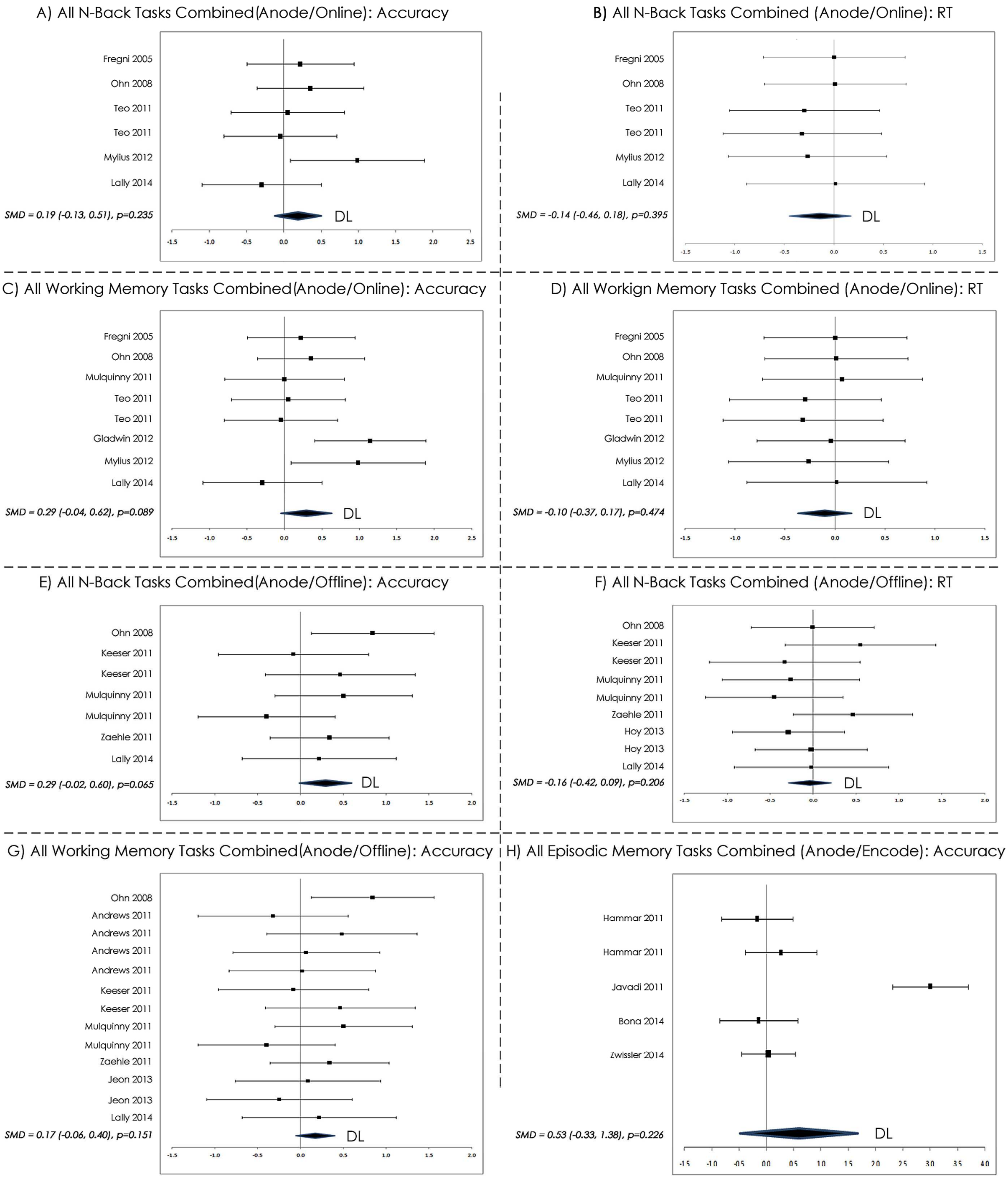


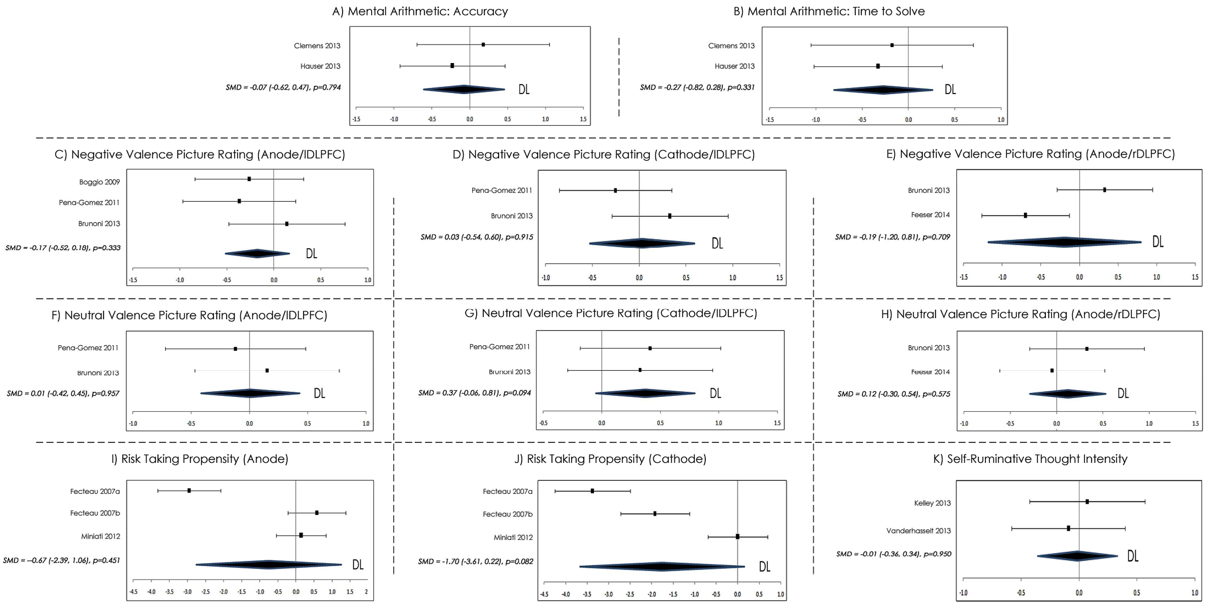
A) Novel Language Learning: Accuracy
Floel 2008
Fiori 2010
SMD = 0.21 [-0.30, 0.73], p=0.416
FE
-1.0
-0.5
0.0
0.5
1.0
1.5
Favors Control
Favors Intervention
B) Picture Naming Task: Reaction Time
Ferratoni 2010
Wirth 2011
SMD = -0.01 [-0.50, 0.48], p=0.979
FE
-1.0
-0.5
0.0
0.5
1.0
Favors Intervention
Favors Control
C) Verbal Fluency (Online): # of Words Generated
Cerruti 2009
Vannorsdaal 2012
Meinzer 2012
SMD = 0.35 [-0.22, 0.91], p=0.226
DL
-1.0
-0.5
0.0
0.5
1.0
1.5
Favors Control
Favors Intervention
D) Verbal Fluency (Offline): # of Words Generated
Cerruti 2009
Cattaneo 2011
Cattaneo 2011
Pennolazzi 2013
Pennolazzi 2013
Pennolazzi 2013
FE
Pennolazzi 2013
SMD = 0.23 [-0.09, 0.55], p=0.160
DL
-1.5
-1.0
-0.5
0.0
0.5
1.0
1.5
2.0
2.5
Favors Control
Favors Intervention


A) Digit Span Working Memory Task: String Length
Andrews 2011
Andrews 2011
Andrews 2011
Andrews 2011
Jeon 2013
Jeon 2013
SMD = 0.01 (-0.34, 0.36), p=0.955
FE
Favors Control
Favors Intervention
B) Verbal Episodic Recognition (Anode): Accuracy
Hammar 2011a
Hammar 2011b
Javidi 2011
SMD = 1.03 (-0.87, 2.94), p=0.235
DL
Favors Control
Favors Intervention
C) Verbal Episodic Recognition (Cathode): Accuracy
Hammar 2011
Hammar 2011
Javidi 2011
SMD = -0.81 (-2.14, 0.51), p=0.230
DL
Favors Control
Intervention
D) Visual Episodic Recognition (DLPFC): Accuracy
Bona 2014
Zwissler 2014
SMD = -0.02 (-0.42, 0.39), p=0.923
DL
Favors Control
Favors Intervention
E) Visual Episodic Recognition (Anode/TEMP): Accuracy
Chi 201
Schaal 2013
SMD = -0.13 (-0.69, 0.44), p=0.660
DL
Favors Control
Favors Intervention
F) Visual Episodic Recognition (Cathode/TEMP): Accuracy
Chi 2010
Schaal 2013
SMD = 0.50 (-0.66, 1.65), p=0.398
DL
Favors Control
Favors Intervention
G) Visual Working Memory (Online): Accuracy
Mulquinny 2011
Gladwin 2012
SMD = 0.57 (-0.55, 1.70), p=0.317
FE
Favors Control
Favors Intervention
H) Visual Working Memory (Online): Reaction Time
Mulquinny 2011
Gladwin 2012
SMD = -0.01 (-0.55, 0.53), p=0.966
FE
Favors Intervention
Favors Control
I) Visual Working Memory (Offline/Anode): Accuracy
Berryhill 2010
Berryhill 2010
Jones 2012
Tseng 2012
Tseng 2012
Hsu 2014
SMD = -0.00 (-0.30, 0.29), p=0.991
FE
Heimrath 2012
Moos 2013
SMD = -0.06 (-0.35, 0.22), p=0.664
DL
Favors Control
Favors Intervention
I) Visual Working Memory (Offline/Cathode): Accuracy
Berryhill 2010
Berryhill 2010
jones 2012
Tanoue 2013
SMD = 0.09 (-0.26, 0.43), p=0.611
FE
Heimrath 2012
Moos 2013
Moos 2013
SMD = 0.03 (-0.22, 0.29), p=0.802
DL
Favors Control
Favors Intervention



A) One-Back Task: Accuracy
Keeser 2011
Mulquinny 2011
SMD = 0.23 (-0.37, 0.83), p=0.447
DL
Favors Control
Favors Intervention
B) One-Back Task: Reaction Time
Keeser 2011
Mulquinny 2011
SMD = 0.12 (-0.67, 0.91), p=0.767
DL
Favors Intervention
Favors Control
C) Two-Back Task: Accuracy
Keeser 2011
Mulquinny 2011
Zaehle 2011
SMD = 0.14 (-0.38, 0.65), p=0.606
DL
Favors Control
Favors Intervention
D) Two-Back Task: Reaction Time
Mulquinny 2011
Hoy 2013
SMD = -0.39 (-0.90, 0.12), p=0.137
FE
Keeser 2011
Hoy 2013
SMD = -0.13 (-0.66, 0.40), p=0.617
FE
Zaehle 2011
SMD = -0.10 (-0.42, 0.23), p=.563
DL
Favors Intervention
Favors Control
E) Three-Back Task (Online): Accuracy
Fregni 2005
Teo 2011
SMD = 0.19 (-0.33, 0.71), p=0.480
FE
Ohn 2008
Teo 2011
SMD = 0.16 (-0.36, 0.69), p=0.541
FE
Lally 2014
SMD = 0.28 (-0.07, 0.62), p=0.112
DL
Favors Control
Favors Intervention
F) Three-Back Task (Online): Error rate
Fregni 2005
Ohn 2008
Lally 2014
SMD = -0.45 (-1.06, 0.16), p=0.148
DL
Favors Intervention
Favors Control
G) Three-Back Task (Online): Reaction Time
Fregni 2005
Teo 2011
SMD = -0.13 (-0.67, 0.40), p=0.631
FE
Ohn 2008
Teo 2011
SMD = -0.14 (-0.67, 0.40), p=0.621
FE
Lally 2014
SMD = -0.11 (-0.46, 0.23), p=0.517
DL
Favors Intervention
Favors Control
H) Three-Back Task (Offline): Accuracy
Ohn 2008
Lally 2014
SMD = 0.58 (-0.03, 1.19), p=0.060
DL
Favors Control
Favors Intervention
I) Three-Back Task (Offline): Error Rate
Ohn 2008
Lally 2014
SMD = -0.24 (-0.83, 0.35), p=0.421
DL
Favors Intervention
Favors Control
J) Three-Back Task (Offline): Reaction Time
Ohn 2008
Lally 2014
SMD = -0.01 (-0.57, 0.55), p=0.967
DL
Favors Intervention
Favors Control

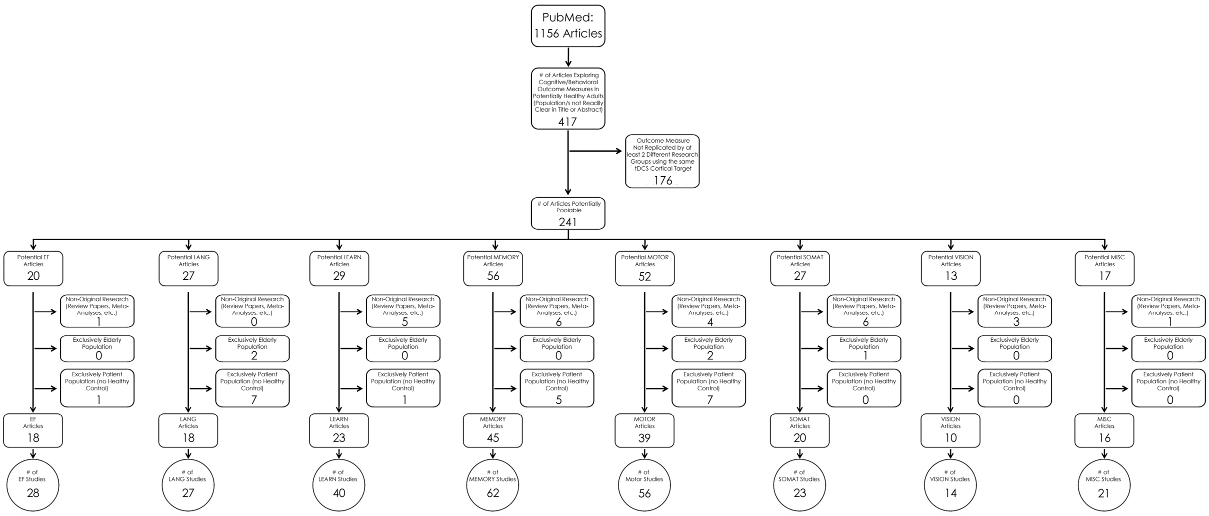

A) All N-Back Tasks Combined(Anode/Online): Accuracy
Fregni 2005
Ohn 2008
Teo 2011
Teo 2011
Mylius 2012
Lally 2014
SMD = 0.19 (-0.13, 0.51), p=0.235
DL
B) All N-Back Tasks Combined (Anode/Online): RT
Fregni 2005
Ohn 2008
Teo 2011
Teo 2011
Mylius 2012
Lally 2014
SMD = -0.14 (-0.46, 0.18), p=0.395
DL
C) All Working Memory Tasks Combined(Anode/Online): Accuracy
Fregni 2005
Ohn 2008
Mulquinny 2011
Teo 2011
Teo 2011
Gladwin 2012
Mylius 2012
Lally 2014
SMD = 0.29 (-0.04, 0.62), p=0.089
DL
D) All Workign Memory Tasks Combined (Anode/Online): RT
Fregni 2005
Ohn 2008
Mulquinny 2011
Teo 2011
Teo 2011
Gladwin 2012
Mylius 2012
Lally 2014
SMD = -0.10 (-0.37, 0.17), p=0.474
DL
E) All N-Back Tasks Combined(Anode/Offline): Accuracy
Ohn 2008
Keeser 2011
Keeser 2011
Mulquinny 2011
Mulquinny 2011
Zaehle 2011
Lally 2014
SMD = 0.29 (-0.02, 0.60), p=0.065
DL
F) All N-Back Tasks Combined (Anode/Offline): RT
Ohn 2008
Keeser 2011
Keeser 2011
Mulquinny 2011
Mulquinny 2011
Zaehle 2011
Hoy 2013
Hoy 2013
Lally 2014
SMD = -0.16 (-0.42, 0.09), p=0.206
DL
G) All Working Memory Tasks Combined(Anode/Offline): Accuracy
Ohn 2008
Andrews 2011
Andrews 2011
Andrews 2011
Andrews 2011
Keeser 2011
Keeser 2011
Mulquinny 2011
Mulquinny 2011
Zaehle 2011
Jeon 2013
Jeon 2013
Lally 2014
SMD = 0.17 (-0.06, 0.40), p=0.151
DL
H) All Episodic Memory Tasks Combined (Anode/Encode): Accuracy
Hammar 2011
Hammar 2011
Javadi 2011
Bona 2014
Zwissler 2014
SMD = 0.53 (-0.33, 1.38), p=0.226
DL


A) Mental Arithmetic: Accuracy
Clemens 2013
Hauser 2013
SMD = -0.07 (-0.62, 0.47), p=0.794
DL
B) Mental Arithmetic: Time to Solve
Clemens 2013
Hauser 2013
SMD = -0.27 (-0.82, 0.28), p=0.331
DL
C) Negative Valence Picture Rating (Anode/lDLPFC)
Boggio 2009
Pena-Gomez 2011
Brunoni 2013
SMD = -0.17 (-0.52, 0.18), p=0.333
DL
D) Negative Valence Picture Rating (Cathode/lDLPFC)
Pena-Gomez 2011
Brunoni 2013
SMD = 0.03 (-0.54, 0.60), p=0.915
DL
E) Negative Valence Picture Rating (Anode/rDLPFC)
Brunoni 2013
Feeser 2014
SMD = -0.19 (-1.20, 0.81), p=0.709
DL
F) Neutral Valence Picture Rating (Anode/lDLPFC)
Pena-Gomez 2011
Brunoni 2013
SMD = 0.01 (-0.42, 0.45), p=0.957
DL
G) Neutral Valence Picture Rating (Cathode/lDLPFC)
Pena-Gomez 2011
Brunoni 2013
SMD = 0.37 (-0.06, 0.81), p=0.094
DL
H) Neutral Valence Picture Rating (Anode/rDLPFC)
Brunoni 2013
Feeser 2014
SMD = 0.12 (-0.30, 0.54), p=0.575
DL
I) Risk Taking Propensity (Anode)
Fecteau 2007a
Fecteau 2007b
Miniati 2012
SMD = -0.67 (-2.39, 1.06), p=0.451
DL
J) Risk Taking Propensity (Cathode)
Fecteau 2007a
Fecteau 2007b
Miniati 2012
SMD = -1.70 (-3.61, 0.22), p=0.082
DL
K) Self-Ruminative Thought Intensity
Kelley 2013
Vanderhasselt 2013
SMD = -0.01 (-0.36, 0.34), p=0.950
DL

Highlights

- Of 42 replicated cognitive outcome measures included in 59 analyses, tDCS has a significant effect on zero
- There appears to be no reliable effect of tDCS on executive function, language, memory, or miscellaneous measures.
- Single-session tDCS does not appear to generate reliable cognitive effect in healthy populations

Supplemental Material



<u>Figure S1</u>: Complete study selection flow-chart. Note: the four arms not discussed in this paper (Learning, Motor, Somatosensory, and Vision) will be explored in a follow-up article.

<u>Table S1</u>: Studies and values for pooled memory task analyses..

Study	N	Active	Ref	Density (mA/cm2)	Task	SMD (95% CI)	Z Value	P Value
N-Back (All Ns Combined) – Anode / Online: **ACCURACY**								
Fregni 2005	15	lDLPFC	rORBIT	0.02857	3-Back	0.31 (-0.41, 1.03)	0.855	0.393
Ohn 2008	15	lDLPFC	rORBIT	0.04	3-Back	0.36 (-0.37, 1.08)	0.966	0.334
Teo 2011	12	lDLPFC	rORBIT	0.02857	3-Back	0.05 (-0.71, 0.81)	0.125	0.901
	12	lDLPFC	rORBIT	0.05714	3-Back	-0.05 (-0.81, 0.71)	-0.128	0.898
Mylius 2012	12	lDLPFC	rORBIT	0.05714	2-Back	-0.30 (-1.10, 0.50)	-0.762	0.468
Lally 2014	9a 10	lDLPFC	rCHK	0.02857	3-Back	0.97 (0.01, 1.92)	1.988	0.047
					DL Model	**0.19 (-0.13, 0.51)**	**1.187**	**0.235**
N-Back (All Ns Combined) – Anode / Online: **RT**								
Fregni 2005	15	lDLPFC	rORBIT	0.02857	3-Back	0.00 (-0.71, 0.72)	0.011	0.991
Ohn 2008	15	lDLPFC	rORBIT	0.04	3-Back	0.01 (-0.70, 0.73)	0.032	0.974
Teo 2011	12	lDLPFC	rORBIT	0.02857	3-Back	-0.30 (-1.11, 0.50)	-0.736	0.462
	12	lDLPFC	rORBIT	0.05714	3-Back	-0.32 (-1.13, 0.48)	-0.781	0.435
Mylius 2012	12	lDLPFC	rORBIT	0.05714	2-Back	-0.27 (-1.07, 0.53)	-0.648	0.517
Lally 2014	9a 10	lDLPFC	rCHK	0.02857	3-Back	0.02 (-0.88, 0.92)	0.037	0.971
					DL Model	**-0.14 (-0.46, 0.18)**	**-0.851**	**0.395**
Working Memory (All WM Tasks Combined) – Anode / Online: **ACCURACY**								

Fregni 2005	15	lDLPFC	rORBIT	0.02857	3-Back	0.31 (-0.41, 1.03)	0.855	0.393
Ohn 2008	15	lDLPFC	rORBIT	0.04	3-Back	0.36 (-0.37, 1.08)	0.966	0.334
Mulquinny 2011	12	lDLPFC	rORBIT	0.0286	STRNBRG	0.000 (-1.62, 0.86)	0.000	1.000
Teo 2011	12	lDLPFC	rORBIT	0.02857	3-Back	0.05 (-0.71, 0.81)	0.125	0.901
	12	lDLPFC	rORBIT	0.05714	3-Back	-0.05 (-0.81, 0.71)	-0.128	0.898
Gladwin 2012	14	lDLPFC	rORBIT	0.0286	STRNBRG	1.14 (0.34, 1.94)	2.803	0.005
Mylius 2012	12	lDLPFC	rORBIT	0.05714	2-Back	-0.30 (-1.10, 0.50)	-0.762	0.468
Lally 2014	9a 10	lDLPFC	rCHK	0.02857	3-Back	0.97 (0.01, 1.92)	1.988	0.047
					DL Model	**0.29 (-0.04, 0.62)**	**1.699**	**0.089**
Working Memory (All WM Tasks Combined) – Anode / Online: **RT**								
Fregni 2005	15	lDLPFC	rORBIT	0.02857	3-Back	0.00 (-0.71, 0.72)	0.011	0.991
Ohn 2008	15	lDLPFC	rORBIT	0.04	3-Back	0.01 (-0.70, 0.73)	0.032	0.974
Mulquinny 2011	12	lDLPFC	rORBIT	0.0286	STRNBRG	-0.07 (-0.87, 0.73)	-0.177	0.859
Teo 2011	12	lDLPFC	rORBIT	0.02857	3-Back	-0.30 (-1.11, 0.50)	-0.736	0.462
	12	lDLPFC	rORBIT	0.05714	3-Back	-0.32 (-1.13, 0.48)	-0.781	0.435
Gladwin 2012	14	lDLPFC	rORBIT	0.0286	STRNBRG	0.04 (-0.70, 0.78)	0.107	0.915
Mylius 2012	12	lDLPFC	rORBIT	0.05714	2-Back	-0.27 (-1.07, 0.53)	-0.648	0.517
Lally 2014	9a 10	lDLPFC	rCHK	0.02857	3-Back	0.02 (-0.88, 0.92)	0.037	0.971
					DL Model	**-0.10 (-0.37, 0.17)**	**-0.715**	**0.474**
N-Back (All Ns Combined) – Anode / Offline: **ACCURACY**								
Ohn 2008	15	lDLPFC	rORBIT	0.04	3-Back	0.84 (0.10, 1.59)	2.214	0.027
Keeser 2011	10	lDLPFC	rORBIT	0.05714	1-Back	-0.08 (-0.96, 0.80)	-0.184	0.854
	10	lDLPFC	rORBIT	0.05714	2-Back	0.46 (-0.43, 1.35)	1.019	0.308
Mulquinny 2011	12	lDLPFC	rORBIT	0.02857	1-Back	0.50 (-0.31, 1.31)	1.206	0.228
	12	lDLPFC	rORBIT	0.02857	2-Back	-0.40 (-1.21, 0.41)	-0.970	0.332
Zaehle 2011	16	lDLPFC	rMAST	0.02857	2-Back	0.39 (-0.36, 1.04)	0.949	0.343
Lally 2014	9a 10	lDLPFC	rCHK	0.02857	3-Back	0.22 (-0.69, 1.12)	0.466	0.641
					DL Model	**0.29 (-0.02, 0.60)**	**1.845**	**0.065**
N-Back (All Ns Combined) – Anode / Offline: **RT**								
Ohn 2008	15	lDLPFC	rORBIT	0.04	3-Back	-0.01 (-0.72, 0.71)	-0.015	0.988
Keeser 2011	10	lDLPFC	rORBIT	0.05714	1-Back	0.55 (-0.34, 1.44)	1.208	0.227
	10	lDLPFC	rORBIT	0.05714	2-Back	-0.741	0.459	-0.741
Mulquinny 2011	12	lDLPFC	rORBIT	0.02857	1-Back	-0.26 (-1.07, 0.54)	-0.638	0.524
	12	lDLPFC	rORBIT	0.02857	2-Back	-0.45 (-1.26, 0.36)	-1.095	0.274
Zaehle 2011	16	lDLPFC	rMAST	0.02857	2-Back	0.46 (-0.24, 1.17)	1.293	0.196
Hoy 2013	18	lDLPFC	rORBIT	0.02857	2-Back	-0.29 (-0.95, 0.37)	-0.868	0.385
	18	lDLPFC	rORBIT	0.05714	2-Back	-0.02 (-0.68, 0.63)	-0.073	0.942
Lally 2014	9a 10	lDLPFC	rCHK	0.02857	3-Back	-0.02 (-0.92, 0.88)	-0.047	0.962
					DL Model	**-0.16 (-0.42, 0.09)**	**-1.266**	**0.206**
Working Memory (All WM Tasks Combined) – Anode / Offline: **ACCURACY**								
Ohn 2008	15	lDLPFC	rORBIT	0.04	3-Back	0.84 (0.10, 1.59)	2.214	0.027
Andrews 2011	10	lDLPFC	rORBIT	0.0286	Forward	-3.22 (-1.21, 0.56)	-0.716	0.474

	10	lDLPFC	rORBIT	0.0286	Backward	0.483 (-0.41, 1.37)	1.065	0.287
	11a / 10s	lDLPFC	rORBIT	0.0286	Forward	0.065 (-0.79, 0.92)	0.148	0.882
	11a / 10s	lDLPFC	rORBIT	0.0286	Backward	0.018 (-0.84, 0.87)	0.040	0.968
Keeser 2011	10	lDLPFC	rORBIT	0.05714	1-Back	-0.08 (-0.96, 0.80)	-0.184	0.854
	10	lDLPFC	rORBIT	0.05714	2-Back	0.46 (-0.43, 1.35)	1.019	0.308
Mulquinny 2011	12	lDLPFC	rORBIT	0.02857	1-Back	0.50 (-0.31, 1.31)	1.206	0.228
	12	lDLPFC	rORBIT	0.02857	2-Back	-0.40 (-1.21, 0.41)	-0.970	0.332
Zaehle 2011	16	lDLPFC	rMAST	0.02857	2-Back	0.39 (-0.36, 1.04)	0.949	0.343
Jeon 2013	8a / 16s	lDLPFC	rORBIT	0.0286	Forward	0.084 (-0.77, 0.93)	0.194	0.846
	8a / 16s	lDLPFC	rORBIT	0.0286	Backward	-0.25 (-1.10, 0.60)	-0.574	0.566
Lally 2014	9a 10	lDLPFC	rCHK	0.02857	3-Back	0.22 (-0.69, 1.12)	0.466	0.641
					DL Model	**0.17 (-0.06, 0.40)**	**1.438**	**0.151**
Episodic Memory (All Tasks Combined) – Anode during Encoding: **ACCURACY**								
Hammar 2011	18	lDLPFC	rORBIT	0.0286	Errorless Learning	-0.17 (-0.82, 0.49)	-0.502	0.616
	18	lDLPFC	rORBIT	0.0286	Errorful Learning	0.268 (-0.39, 0.92)	0.800	0.424
Javadi 2011	16	lDLPFC	rORBIT	0.0816	-	3.00 (1.99, 4.01)	5.821	<0.001
Bona 2014	15	lDLPFC	rORBIT	0.0286	Cued Learning	0.037 (-0.45, 0.53)	0.146	0.884
Zwissler 2014	24a / 48s	lDLPFC	rDELT	0.0571	-	-0.14 (-0.86, 0.58)	-0.385	0.700
					DL Model	**0.53 (-0.33, 1.38)**	**1.211**	**0.226**

Table S2: Complete list of studies that explored an outcome measure included in our quantitative review, but which targeted a neural region not replicated by a second research group.

Task - Stimulation	Paper	Cortical Target
Set Shifting - Anode/Offline	[1]	M1
Stop Signal - Anode/Offline	[2]	MFC
	[3]	rAG
Stroop Task – Anode/Offline	[4]	aPFC
	[5]	M1
	[6]	Bilateral PPC
Novel Language Learning Task – Anode/Offline	[7]	Broca's
	[8]	M1
	[9]	PFC
Picture Naming Task – Anode/Offline	[10]	rIFG
Picture Naming Task – Anode/Online	[11]	Temporal Lobe
	[12]	IFG
Picture Naming Task – Cathode	[11]	Temporal Lobe
	[13]	lDLPFC
	[10]	IFG

Digit Span Working Memory Task – Anode/Offline	[14]	Parietal Cortex
	[15]	Cerebllum
	[16]	rDLPFC
Verbal Episodic Memory – Anode/Encoding	[17]	Temporal Cortex
	[18]	M1
	[19]	Parietal Cortex
Verbal Episodic Memory – Anode/Retrieval	[20]	Parietal Cortex
Visual Episodic Memory – Cathode/Encoding	[21]	lDLPFC
Visual Episodic Memory – Anode / Online	[22]	lDLPFC
Visual Episodic Memory – Anode / Offline	[23]	lDLPFC
Visual Working Memory – Anode/Offline	[24]	lDLPFC
Visual Working Memory – Cathode/Offline	[25]	rDLPFC
N-Back Working Memory	[26]	M1
	[27]	rParietal Cortex
	[28]	lParietal Cortex
	[15]	Cerebellum
Mental Arithmetic – Anode/Offline	[29]	Cerbellum
	[30]	lParietal Cortex
	[6]	Bi-Lateral Parietal Cortices
Picture Viewing/Rating – Anode/Online	[31]	M1
	[31]	V1
Additional Omissions		
Visual Working Memory – Anode/Online	[32]	Utilized a Pulsed-tDCS Paradigm (not continuous current)
Notes: M1 = Primary motor cortex; MFC = Medial Frontal Cortex; rAG = Right angular gyrus; aPFC = Anterior prefrontal cortex; PPC = Posterior parietal cortex; PFC = Prefrontal cortex; IFG = Inferior frontal gyrus; DLPFC = Dorsolateral prefrontal cortex; V1 = Primary visual cortex.		

Table S3: Outcome measures not included in this quantitative review due to lack of intra-group replication

Task	# of Studies	Notes:
9-Dot / 4-Line Task	1	-
Aesthetic Appreciation Task	1	-
Anti-Saccade Task	2	Different active electrode locations
Associative Object location Learning	1	-

Attentional Alerting Task	1	-
Attentional Orientation Task	1	-
Auditory Emotional Prosody Task	1	-
Auditory Frequency Discrimination Task	2	1 did not supply enough information to derive an effect size
Auditory Gap Detection Task	2	Different active electrode locations
Auditory Pitch matching Task	1	-
Biological Motion Perception	1	-
Choice Reaction Time Task	7	1 utilized an elderly population, 1 utilized a 4-day training regimen (no data for day 1 only), the remaining 5 each utilized different active electrode locations
Color Discrimination Task	1	-
Columbia Card Task	1	-
Degraded Speech interpretation Task	1	-
Delayed Discounting Task	1	-
Driving Style	1	-
Dynamic Mechanical Allodynia	2	1 did not report quantitative data
Error Awareness Task	2	1 utilized an elderly population
Facial After-Effect Adaptation	1	-
Facial Attractiveness Task	1	-
Facial Emotion Recognition Task	2	Different active electrode locations
Finger Tapping Speed	3	Different active electrode locations
Flanker Task	3	Different active electrode locations
Flexible Tool-Use Task	1	-
Free Choice Preference Change Task	1	-
Gait and Posture Task	1	-
Gambler's Fallacy Task	1	-
Gesture Processing	1	-
Go-No Go: Linguistic	2	Different active electrode locations
Go-No-Go: Basic Motor	1	-
Go-No-Go: Emotional	3	1 utilized a non-comparable masking paradigm whilst 1 utilized a non-comparable priming paradigm
Go-No-Go: Parametric	1	-
Go-No-Go: Stroop	1	-
Grooved Peg-Board Task	6	1 did not include a sham condition, 1 *only* used a sham condition, 1 used an elderly population, 1 did not include quantitative data, and the remaining 2 used different active

		electrode locations
Human Endowment Effect	1	-
Local/Global Visual Processing	2	1 utilized a non-comparable salience-based paradigm
Lucid Dreaming	1	-
Maze/Trail Completion	2	1 did not include numeric data
Mental Body Representation	1	-
Model-Based Learning Task	1	-
Moral Judgment Task	2	Different active electrode locations
Motion After-Effect	1	-
Motor Surround Inhibition Task	1	-
Multi-Tasking	1	-
Novel Numerical Learning Task	1	-
Orientation Discrimination Task	3	1 utilized a different active electrode location, the remaining two are from the same research group
Pain Perception: Electrical Stimulation	2	Non-comparable outcome measures (threshold vs discomfort rating)
Pain Perception: Laser Stimulation	3	All from same research group
Paradoxical Heat Sensation	2	1 did not report quantitative data
Perceived Exertion during Cardio Activity	1	-
Phosphene Detection	1	-
Phosphene Threshold	6	1 did not include a sham condition, the remaining 5 are from the same research group
Posner Paradigm - Endogenous Cue	3	1 utilized a different active electrode location, the remaining two are from the same research group
Posner Paradigm - Exogenous Cue	1	-
Presence Task	1	-
Probabilistic Classification Learning Task	1	-
Probabilistic Guessing Task	1	-
Pro-Saccade Task	1	-
Punishment Determination Task	1	-
Random Number Generation Task	1	-
Reality Filtering	1	-
Retrieval induced	1	-

Forgetting task		
Selective Attention task	1	-
Self-Motion Perception	1	-
Semantic Congruency Task	4	All same research group
Semantic Dissonance Task	4	1 utilized a different active electrode location, the remaining 3 are all the same research group
Semantic Idiom Task	1	-
Semantic Interference Paradigm	3	1 utilized an offline protocol, the remaining 2 (both online) utilized different active electrode locations
Semantic Priming Task	2	Different active electrode locations
Semantic Priming Task - Faces	1	-
Semantic Priming Task - Verbal	2	Same research group
Sequential Reaction Time Task	1	-
Social Anger Task	1	-
Social Cognition	1	-
Social Norm Compliance	1	-
Spatial Orientation Task	1	-
Spontaneous Verbal Response Task	2	Different active electrode locations
Stimulus-Response Binding	1	-
Strength Training Task	1	-
Stress Response	1	-
Sustained Attention Response Task	1	-
Swallowing Task	2	1 exclusively combined tDCS with rTMS
Tactile Localization	3	1 utilized a different active electrode location, the remaining two are from the same research group
Temporal Auditory Processing	1	-
Temporal Causality Task	1	-
Threat Detection Task	4	All same research group
Time Interval Estimation task	1	-
Tongue Twister Task	1	-
Top-Down Visual Attention Task	1	-
Tower-of-London Task	1	-
Verbal Association Task	2	1 utilized an online protocol, 1 an offline protocol
Verbal Episodic Memory - Recall	4	1 did not report any variance data, 1 utilized a non-comparable cued-recall paradigm, 1 utilized a 10-day training paradigm (no Day 1 data)
Verbal Generation Task	2	Both same research group

Verbal Insight Problem Task	1	-
Verbal Long Term Memory	1	-
Vigilance Task	1	-
Visual (Matchstick) Insight Problem Task	1	-
Visual Change Detection/Blindness	2	Different active electrode locations
Visual Episodic Memory - Recall	2	Different active electrode locations
Visual Item Categorization task	1	-
Visual Search Task	1	-
Visual Surround Suppression	1	-
Visual Target Discrimination	5	1 utilized a non-comparable implicit learning/stop-signal paradigm whilst the remaining 4 utilized different active electrode locations
Woodcock Reading Mastery Task	1	-
Word Reading Efficiency	3	1 utilized a 10-day training paradigm (no Day 1 data), the remaining 2 utilized different active electrode locations

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